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Lausanne (Switzerland), September 5–6, 2024

ABSTRACTS OF THE ANNUAL MEETING OF THE SWISS SOCIETY OF RHEUMATOLOGY

LAUSANNE, SEPTEMBER 5–6, 2024

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BEST ABSTRACTS

Best abstract 1

Anti-Ro/SSA antibodies are predictive of more severe lung involvement in patients with systemic sclerosis: a study from the EUSTAR database

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Background: Despite the progress in explaining the clinical heterogeneity in systemic sclerosis (SSc) based on SSc-specific antibodies, better understanding of additional risk factors is needed. SSc non-specific antibodies might represent additional markers to improve the stratification of SSc patients.

Objective: We aimed to evaluate the prevalence of anti-Ro/SSA antibodies in the EUSTAR database and study their association with disease phenotype and clinical outcomes, focusing on lung involvement.

Methods: SSc patients from the EUSTAR database with available data on anti-Ro/SSA antibodies, were included. Clinical characteristics of patients with or without anti-Ro/SSA antibodies were compared at baseline. Multivariable logistic regression models were built to identify factors associated with lung fibrosis. The progression of lung fibrosis was defined by FVC% decline from baseline of ≥ 10% or a FVC% decline of 5-9% in association with a DLco% decline of ≥15% or by a decline of FVC >5% in patients with lung fibrosis or by the development of lung fibrosis de novo. Prognostic factors for progression of lung fibrosis and death during follow-up were tested by multivariate Cox proportional hazards regression.

Results: Among the 4'421 patients fulfilling the inclusion criteria, 661 (15.2%) had positive anti-Ro/SSA antibodies. Anti-Ro/SSA antibodies were positively associated (p <0.001) with anti-SSB, anti-U1RNP antibodies, and rheumatoid factor. Patients with anti-Ro/SSA antibodies more frequently presented with muscular involvement (18% vs 12.5%, p <0.001), and lung fibrosis (56.2% vs 47.8%, p = 0.001) at baseline. Over a median follow-up of 2.7 years,14'066 visits were recorded. In multivariable logistic regression, anti-SSA independently predicted the presence of lung fibrosis in at least one follow up visit (OR 1.24, p = 0.006) and lower DLCO in patients with lung fibrosis (regression coefficient: -1.9, p = 0.049). Anti-SSA antibodies had a trend to predict lower FVC in patients with lung fibrosis (p = 0.082). Anti-SSA antibodies did not predict the progression of lung fibrosis or death during the follow-up.

Conclusions: Anti-SSA antibodies are detected in 15% of SSc-patients and represent an independent risk factor for the presence of lung fibrosis. They are also predictive of more severe lung involvement. These data support the inclusion of anti-SSA antibodies in routine clinical practice to improve the risk-stratification of SSc patients.

Best abstract 2

Synovitis in Systemic Sclerosis is Characterised by an Interferon Signature

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In lack of evidence-based therapies, systemic sclerosis (SSc) patients with synovitis are treated as rheumatoid arthritis (RA) patients, yet with unknown effect. Thus, we aim to decipher the histological, cellular, and transcriptional differences between SSc and RA synovitis, specifically in synovial fibroblasts (SF).

We collected ultrasound-guided synovial biopsies of 11 SSc and 7 RA patients. All samples were analysed histologically, including Krenn synovitis score (0-9) and pathotype characterisation. Additionally, 7 SSc and 6 RA samples were dissociated and processed for single-cell RNA-sequencing (20,705 cells in SSc and 31,681 in RA). Given the mainly pauci-immune pathotype of the SSc synovitis, we focused our analysis on the different SF clusters (SSc: 4638; RA: 6097 cells), performed differential gene expression, pathway analysis and compared with the transcriptional profiles of in vitro stimulated SF.

The Krenn synovitis score was lower in SSc than in RA (2.1±1.4 vs. 4.2±1.0, p = 0.01) and SSc pathotypes were mainly pauci-immune (91% vs. 43% of RA biopsies, p = 0.04). Consistently, neutrophils were more prevalent in RA as compared to SSc synovitis (p < 0.01).

On the single-cell level, we identified seven SF clusters expressing the marker genes PRG4, CHI3L2, COMP, CXCL12, CXCL14, MFAP5, and POSTN. MFAP5+ (Fold-change (FC) = 3.81, false discovery rate (FDR)<0.001) and COMP+ (FC = 2.28, FDR<0.001) SF were more abundant in SSc, while CXCL12+ and POSTN+ SF were more prevalent in RA. Between SSc and RA SF we found 675 significant differentially expressed genes (FDR<0.01, $|\log2FC|>0.25$) and several differentially activated signalling pathways. In particular, SSc SF were enriched in IFNα and IFNγ (both FDR<0.018) and complement and coagulation pathways (FDR<0.008), especially in genes of the alternative complement pathway (e.g. CFD, CFH). In RA, SF genes of the TNFα signalling pathway (FDR < 6.3e-12) and inflammatory response genes (FDR<0.018) were most over-represented. In the transcriptomic profile of in vitro stimulated SF, IFN led to a similar upregulation of alternative complement genes as seen in SSc SF.

This first in-depth characterisation of SSc synovitis revealed hallmark differences to RA. We confirmed a pauci-immune histopathology and found an upregulation of genes in the IFN signalling pathway in SSc SF, possibly leading to a dysregulation of the alternative complement pathway. This suggests a potential new target of intervention in SSc synovitis.

Best abstract 3

Accumulation of T cells in Modic type 1 changes that recognize stress-induced molecules

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Background: Modic type 1 changes (MC1) are vertebral bone marrow lesions adjacent to degenerating intervertebral discs and have a high specificity for diskography concordant pain. Endplate damage associates with MC1, exposing the immune-privileged disc to immune cells of the adjacent bone marrow. Whilst local inflammation is a hallmark of MC1, immune system remodeling in MC1 lesions is poorly understood.

Objective: To investigate changes in the bone marrow immune cell composition in MC1.

Methods: Vertebral bone marrow aspirates (n = 22, MC1+intra-patient control = 8+8, control patients = 6) were obtained from spinal fusion patients. Mononuclear cells were analyzed by a 36-color flow cytometry-based immunophenotyping panel combined with 360 PE-labeled antibodies against surface markers. To avoid batch effects, each sample was barcoded with a unique combination of fluorescently labeled anti-CD45 antibodies, and all samples were analyzed in one tube. Data was computationally demultiplexed, gated into immune cell populations, and the expression of screened markers on the surface of these populations was analyzed. Two types of analyses were done: (i) MC1 vs. control patients, (ii) MC1 lesions vs. intra-patient controls.

Results: NK-like T cells and TCR Vδ1+ T cells were enriched in MC1 vs. control patients (NK-like T cells: +170%, p = 0.022; TCR Vδ1+ T cells: +93%, p = 0.030) and in MC1 vs. intra-patient bone marrow lesions (NK-like T cells: +29%, p <0.001; TCR Vδ1+ T cells: +15%, p <0.001). Effector memory cells (TEM [CCR7-CD45RA-], TEMRA [CCR7-CD45RA+]) accumulated in MC1 vs. control patients (TEM: +32%, p<0.006; TEMRA: +27%, p = 0.35) and in MC1 vs. intra-patient controls (TEM: +6%, p <0.001; TEMRA: +9%, p = 0.001), suggesting ongoing stimulation of T cells. Infiltrating T cells expressed more of the stress-molecule receptors NK receptors NKG2D (+15%, p <0.001) and NKp80 (+9%, p = 0.031). Expression of NKG2D was among all T cell subsets highest on TCR Vδ1+ T cells, NKp80 was highest on NK-like T cells, suggesting that recognition of stress-induced molecules could trigger accumulation of these T cell subsets in MC1.

Conclusion: This ex vivo analysis provides the first direct evidence of specific T cell subset accumulations in MC1. Particularly, NK-like T cells and TCR Vδ1+ T cells are accumulated in MC1 and have with the potential to react to stress-induced molecules. Understanding the role of these T cell subsets may be a key step toward designing targeted treatments for MC1.

BEST CASES

Best case 1

Rare cause of musculoskeletal pain in a young male adult

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A 19-year-old man with no previous medical history presented to his general practitioner with sore throat, diffuse hair loss and fever, followed two weeks later by neck pain and bilateral hip and shoulder pain for the past two months. Symptomatic treatment without antibiotics for suspected pharyngitis and tonsillitis did not lead to any improvement. Joint pain worsened in the morning and during physical exertion and was refractory to NSAIDs. There were no abnormalities in the MRI scan of his left hip, so the joint pain was attributed to his football training, which he practiced six times a week. Due to persistent symptoms, he was referred to our rheumatology clinic. The clinical examination revealed bilateral purulent tonsillitis and palpable cervical, axillary, and inguinal lymph nodes, that were firm and painless. He had discrete papules at the PIP and DIP joints of both hands. Joint examination itself was unremarkable. Sexual history revealed unprotected sexual intercourse with four different women in the last months, the last time three months before the consultation. Clinical examination of the genital region showed a circular erythema on the dorsum of the penis (5-10 mm in diameter) and several white dots on the scrotum. Lab results showed elevated inflammatory markers (CRP 24 mg/l, leukocytes 8.0 G/l, ESR 65 mm/h), the rheumatoid factor IgM was 3 times over ULN, the ANA titre was 1:80, HIV and hepatitis screening were unremarkable. However, the anti-Treponema pallidum Ig Antibody Test was positive and the Treponema pallidum hemagglutination assay (TPHA) was highly positive (1:10240). To determine disease activity, the rapid plasma reagin test (RPR) was performed which was also highly reactive (1:256). Secondary syphilis was diagnosed and treated together with the infectious diseases division with three intramuscular injections of benzathine penicillin 2.4 million units, each administered once a week. After treatment, all symptoms completely disappeared and the RPR normalized (1:1) within 6 months of treatment. In conclusion, we report a case of secondary syphilis, which initially presented as tonsillitis, followed by neck pain, arthralgias of big joints and skin efflorescence. Syphilis should be considered as differential diagnosis of arthralgias, if there is a history of sexual contacts, lymphadenopathy and/or symptoms consistent with infectious disease.

Best case 2

Pulmonary infiltrates as initial manifestation of polyarteritis nodosa

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Polyarteritis nodosa (PAN) is a necrotizing angiitis that may present with fever, weight loss, cutaneous and musculoskeletal symptoms. Involvement of gastrointestinal and renal arteries may result in bleeding and ischemic complications. Therefore, early diagnosis and initiation of immunosuppressive therapy may ameliorate the course of disease.

We here report on a previously healthy 55-year-old male who presented with fever up to 40°C. Laboratory analysis revealed elevated inflammatory parameters (CRP 366 mg/l, BSR > 130 mm/h) and leucocytosis (15-23 G/l). The detection of pulmonary infiltrates on chest x-ray prompted initiation of amoxicillin. After 4 days, he was admitted to our hospital because of ongoing fever, night sweats and holocephalia with photophobia. No abnormal findings were detected in the cerebrospinal fluid.

A PET-CT did not reveal any malignancy, abscess formation or large vessel vasculitis. However, mild pulmonary FDG uptake was noted and considered to represent pulmonary inflammation. An extensive microbial workup including bronchoscopy and a bilateral video assisted thoracoscopic surgery wedge biopsy was not able to identify any specific pathogen.

During follow-up, worsening of anemia (from Hb 107 g/l to Hb 82 g/l) and proteinuria (1.09 g/day without erythrocyturia) with persistent fever and chills were noted. Blood pressure remained normal.

Three weeks after onset of fever, the patient suddenly developed severe abdominal pain, tachycardia and hypotension. An abdominal CT scan revealed intraabdominal bleeding from the left kidney that extended into the retroperitoneum and the into the pelvic region. Occlusion of the lienal artery with almost abrogated perfusion of the spleen was detected. Emergency angiography revealed a fulminant generalised arteriopathy with multiple pearl-like aneurysms and dissections. A ruptured aneurysm emanating from a branch of the left inferior renal artery was identified as the cause of bleeding. Coiling was successful and bleeding was stopped.

High dose methylprednisolone and iv cyclophosphamide were started and a decrease of CRP and ESR was noted. Deficiency of adenosine deaminase type 2 was not detected. The patient received a total of 12 (monthly) cyclophosphamide infusions (11.6 g) while prednisone was tapered to 5mg daily that lead to partial remission. Thereafter, a regimen of tocilizumab 8 mg/kg body weight i.v. every 4 weeks was started that lead to complete remission and allowed withdrawal of prednisone.

Best case 3

Dual cytokine targeting with ustekinumab and golimumab for long-standing, treatment-refractory enteropathic spondyloarthritis: A case report

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Combining biologics directed against different cytokines represents a conceptually attractive option in patients with refractory inflammatory diseases. However, previous studies combining a TNF inhibitor with either anakinra or abatacept resulted in a higher rate of infectious complications without increasing clinical efficacy.

We here report on a 31-year-old male patient with axial and peripheral spondyloarthritis associated with ulcerative colitis that was diagnosed in 2005. Due to a refractory disease course, the patient underwent proctocolectomy with ileoanal anastomosis (J-pouch) in 2013. In 2021, a phenotypic switch to Crohn's disease was noted as the patient developed ileitis proximal of the pouch and perianal fistula.

Immunosuppressive regimen comprised of long-term glucocorticoid therapy, in addition, azathioprine, salazopyrine, infliximab, adalimumab, and certolizumab pegol were used, while concomitant osteoporosis and adrenal insufficiency developed. In September 2022, a severe flare with pouchitis, cuffitis, inflammation of the anastomosis site, progression of fistula formation, accompanied by exacerbation of axial and peripheral spondyloarthritis occurred. Daily prednisone was increased to 30 mg and ustekinumab at a dose of 390 mg iv followed by 90 mg sc every 8 weeks was started and lead to an improvement of the inflammatory bowel disease. However, axial and peripheral spondyloarthritis persisted and MRI revealed active sacroiliitis with new erosions of the sacroiliac joints and arthritis of the costovertebral joints. Arthritis of the right ankle was confirmed clinically and by ultrasound.

As the patient refused a cessation of ustekinumab, a consensus decision was made to start dual biologic therapy with ustekinumab and golimumab in August 2023.

Initially BASDAI was 6.4, ASDAS 5.0; in October 2023, BASDAI and ASDAS decreased to 0.65 and 1.2 indicating remission.

Since then, the patient maintained in stable remission with regard to both inflammatory bowel disease and spondyloarthritis. Improvement of adrenal insufficiency and DXA was noted. Furthermore, no side effects and no increase in infections of this dual anti-cytokine directed biologic therapy were observed.

Best case 4

Purpuric rash, fever and arthritis: it is not always a vasculitis

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We present the case of a 47-year-old woman who was hospitalized as she presented with a week-long history of malaise, fevers, night sweats, arthralgias, and diarrhoea. She rapidly developed a purpuric rash on her legs, extending to her upper limbs within a day. She reported diffuse muscle weakness, predominantly affecting her lower limbs and hands, knees and ankles, and joint pain. Intriguingly, two of her children had experienced similar symptoms three weeks prior, albeit without cutaneous rash or muscle weakness.

On clinical examination, the patient demonstrated diminished general condition without fever. We observed psychomotor slowing and moderate tetraparesis, primarily affecting the lower extremities. She exhibited a palpable purpuric rash with a glove-and-stocking distribution, affecting both upper and lower limbs. Oligoarthritis involving the wrists, knees, and ankles was noted.

Joints, chest X-ray and cerebral angio-MRI were normal. Musculoskeletal ultrasonography confirmed effusion of ankles, knees, and right wrist. Laboratory tests showed inflammation (CRP 28 mg/l, ESR 59 mm/h), mild lymphopenia and anaemia. Urine testing showed proteinuria (urine protein/creatinine ratio: 57 g/mol) without leukocyturia or hematuria. ANCA, anti-PR3, and anti-MPO, RF were negative. Skin punch biopsy showed nonspecific leukocytoclastic vasculitis, and IgA staining was negative. Knee aspiration confirmed an inflammatory synovial fluid, and the culture was sterile. Serological tests revealed acute Parvovirus B19 infection (IgM+, IgG+) and a possible acute FSME infection (IgM+, IgG borderline) despite previous vaccination against tick-borne encephalitis. Screening for B. burgdorferi, T. pallidum was negative. PCR assays were positive for Parvovirus B19 in both blood and synovial fluid.

We concluded that the most likely diagnosis was acute infection with Parvovirus B19 with multisystemic manifestations. IgM positivity for tick-borne encephalitis was considered incidental with clinical resolution predominantly attributed to Parvovirus B19 infection.

The patient experienced clinical and biological improvement in one week and was discharged with complete resolution of symptoms with symptomatic treatment only.

This case underscores that a viral infection can mimic severe systemic diseases, such as vasculitis, and highlights the current parvovirus B19 epidemic in our region. Parvovirus B19 infection should be considered in patients presenting with acute fever and arthritis.

Best case 5

Look for the zebra: Lipoma arborescens – a rare cause of a monoarthritis (case report)

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Juvenile idiopathic arthritis (JIA) is the most common chronic childhood arthritis and is a diagnosis of exclusion; therefore other inflammatory and non-inflammatory diseases have to be considered.

We here describe a 25-year-old male patient who was referred to us with refractory JIA that had been diagnosed at the age of two. He presented with persistent polyarthritis despite many previous treatments. At the age of 5, treatment with etanercept was initiated, but was discontinued two years later due to persistent remission. After years of drug-free remission he experienced a relapse at the age of 20. Despite the use of etanercept, golimumab, upadacitinib, abatacept and methotrexate, remission was not achieved.

When the patient presented to us for the first time, arthritis was present in both wrists and both knees. We started tocilizumab and achieved a partial response with arthritis in the wrists and the left knee responding well to the therapy. However, monoarthritis in the right knee persisted. An ultrasound examination of the right knee revealed extensive synovial hypertrophy with multiple synovial villi. Swelling and pain persisted despite an intraarticular injection with triamcinolone. An MRI was performed and confirmed synovial hypertrophy with partial lipomatous transformation. We decided to perform a diagnostic and therapeutic arthroscopy with an extensive synovectomy. Intraoperative findings revealed a lipoma arborescens, which was confirmed histologically. After the synevectomy the patient struggled with a postoperative hemarthrosis, but two months later there was a clear clinical improvement with reduced swelling and less pain.

Lipoma arborescens is a rare cause of a monoarthritis. In patients with an unusual clinical presentation or course of disease despite the use of various biologic DMARDs and/or JAK inhibitors, alternative causes should be considered despite a previously established diagnosis.

Best case 6

Erdheim Chester Disease complicated by Granulomatous Polyangiitis

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Background: First documented case of a patient developing PR3 ANCA+ granulomatous polyangiitis (GPA) following Erdheim-Chester disease (ECD), a clonal myeloid disease leading to multisystemic inflammation characterized by histiocytes harboring mutations in the MAP-kinase pathway most often the BRAF VE600 but also NRAS and KRAS.

Case description

A 66-year-old man presented with acute right thoracic pain, systemic inflammation and renal insufficiency (GFR 41ml/min/1.7) with active urine sediment. PET/CT showed bilateral pleural effusions, lung consolidations, and paravertebral infiltration of the perirenal spaces. Kidney biopsy confirmed pauci-immune glomerulonephritis with crescents and paravertebral biopsy a fibrotic, xanthogranulomatous inflammatory reaction and focal necrotizing vasculitis with associated granuloma (ECD was mentioned as a differential diagnosis). Serology was positive for PR3 ANCA (>177U/ml). The patient was diagnosed with GPA and treated with prednisone and rituximab followed by methotrexate maintenance. Renal function normalized, PR3 decreased to 22U/ml. Chest pain and mild systemic inflammation persisted. PET/CT scan 5 months thereafter showed metabolic response of all lesions except the thoracal manifestation and FDG uptake in both tibiae (not included in the first scan).

Knee MRI, in 2009, due to pain showed bilateral, symmetric metaphyseal and diaphyseal sclerosis, typical for ECD. The diagnosis was not made and afterwards the patient was asymptomatic.

NGS of the paravertebral tissue revealed a known pathogenic p.Q61R NRAS mutation in exon 3. Typical MRI, PET/CT and histological findings finally led to the diagnosis of ECD. Due to incomplete response to immunosuppressive therapy Trametinib, a specific inhibitor of the MAP kinase pathway, was added(1) and led to a rapid clinical response.

Conclusion: Vasculitis is a known complication of other clonal haematological diseases e.g. myelodysplastic diseases(2). Immune pathology of GPA involves the MAP-kinase pathway(3). Altered presentation of proteinase-3 by mutated histiocytes in the context of an activated, mutated MAP-kinase pathway may have promoted the development of GPA in our patient. Whether treatment of ECD with Trametinib alone is sufficient to control GPA has to be awaited.

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BEST ABSTRACTS IN BASIC RESEARCH

Basic research 1

Macrophage extracellular traps induced by monosodium urate or calcium pyrophosphate crystals form independently of NLRP3 inflammasome activation

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Monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals are potent inducers of inflammation. They activate the inflammasome in neutrophils which undergo cell death by extracellular trap formation (NETosis), resulting in flares of gout or pseudogout. However, crystal deposition does not always lead to inflammatory flares; homeostatic mechanisms prevent inflammasome activation.

Here, we investigate the role of macrophages' extracellular trap (MET) formation stimulated with MSU and CPP crystals.

MET formation was assessed in PMA differentiated THP-1 cells, and human monocytes from healthy donors, isolated by magnetic bead separation and differentiated in vitro with GM-CSF or M-CSF, respectively, to obtain M1 and M2 macrophages. Macrophages were stimulated in vitro with MSU and CPP crystals with or without priming with IFNg/LPS. METs were detected by DNA staining with SytoxGreen and anti-citH3/MPO antibodies; an automated imaging system quantified the stainings. IL-1b production was measured by ELISA. Macrophages were stimulated in the presence or absence of NLRP3 and Caspase 1 inhibitors and in THP-1 cells deficient for NLRP3 and gasdermin D (GSDMD). In addition, METs were assessed in peritoneal cavity macrophages of C57BL6/c and Caspase-1/-11, NRLP3 and GSDMD- KO mice.

THP-1 cells released MET after both MSU and CPP crystal stimulation independent of priming with LPS/IFNg. Crystal stimulation of primary human monocytes did not lead to MET formation, but in vitro differentiated M1 and M2 macrophages released MET. In contrast, crystals alone did not result in IL-1b production but required LPS/IFNg priming in M1 macrophages, whereas M2 did not secrete IL-1b. Pharmacological inhibitors of NLRP3 and Caspase 1/4 did not inhibit MET formation after crystal stimulation. Likewise, MET were found in crystal-stimulated THP-1 cells deficient for NLRP3 and GSDMD. To assess MET formation in tissue-resident macrophages, peritoneal cavity macrophages from mice were utilized; METs could be detected in wild type, as well as NLRP3, Caspase-1 and GSDMD deficient mice macrophages, documenting independence of inflammasome activation.

MSU and CPP crystal-induced formation of MET. METosis was independent of inflammasome activation. IL-1b production required priming with LPS/IFNg. These results suggest that METosis may represent an alternative non-inflammatory mechanism by which macrophages may trap crystals without provoking pyroptosis and inflammatory flares.

Basic research 2

CHI3L1 and CHI3L2 represent two highly specific synovial fibroblast-related biomarkers in both seropositive and seronegative rheumatoid arthritis.

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Chronic inflammatory joint diseases are often difficult to diagnose due to their overlapping clinical presentations and lack of specific diagnostic tests. Distinguishing rheumatoid arthritis (RA) from psoriatic arthritis (PsA) or undifferentiated arthritis (UA) is crucial because of their different underlying pathogenic mechanisms and therefore distinct therapeutic strategies. Serological markers, such as Rheumatoid factor (RF) and Cyclic citrullinated peptide antibodies (anti-CCP), has been pivotal in diagnosing RA. However, approximately 5% of PsA patients are seropositive for anti-CCP, while approximately 20% of RA patients remain seronegative for both RF and anti-CCP. This underscores the need for additional disease-specific biomarkers. Ten SF subpopulations were identified – two subpopulations of lining SF, five sublining, two subpopulations of intermediate SF (expressing both lining and sublining markers), and a subpopulation of proliferating fibroblasts. Patients with RA had a higher proportion of CHI3L2high SF than patients with other diagnoses and healthy controls (mean proportion RA = 8.1% (±8.2) vs other = 1.9% (±4.6%)). The proportion did not correlate with any clinical characteristics. Analysis of differentially expressed genes showed CHI3L1 and CHI3L2 had significantly higher expression in RA compared to other types of inflammatory arthritis and healthy controls (p-value adjusted < 0.001). We found no significant differences in the expression of CHI3L1 and CHI3L2 between seropositive and seronegative patients with RA and no correlation with other clinical characteristics. Analysis of CHI3L1 expression in an additional scRNAseq dataset [Floudas et al., 2022] also showed higher expression of the genes in RA patients compared to PsA in SF. The concentration of CHI3L1was significantly higher in the serum of RA patients compared to PsA in a different cohort of patients (mean conc. RA = 183.7 ng/mL (±87.3), mean conc. PsA = 48.7 ng/mL (±25.8) adj. p-value = 0.004). Discrimination between RA and PsA diagnosis using logistic regression based only on CHI3L1 serum levels showed a mean AUC of 0.931 (±0.12) characterizing CHI3L1 as a sensitive and specific peripheral biomarker for RA. In conclusion, the concentration of CHI3L1 in the serum of RA patients was significantly higher than in PsA patients and high enough to be detected through methods routinely employed in clinical and laboratory settings.

Basic research 3

Myosin II (NMII) isoforms contribute to TGFβ-driven fibrosis in SSc

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Background: Systemic sclerosis (SSc) is an autoimmune disease marked by fibrosis in the skin and other organs, leading to severe disability and diminished quality of life. Current therapies manage symptoms but lack the ability to halt or reverse fibrosis. Recent research highlights mechanotransduction pathways, converting mechanical forces into cellular signals, as crucial for fibrosis. These pathways influence the properties of the ECM. Notably, the Rho/ROCK pathway, involving Rho GTPase and ROCK 1 and 2 kinases, activates non-muscle myosin II (NMII), essential for cell contractility. Despite its link to fibrosis, the specific role of NMII isoforms (NMIIA and NMIIB) and their interaction with TGFβ, a key profibrotic mediator in SSc, remain unclear. Deciphering these mechanisms is vital for developing antifibrotic therapies.

Methods: We investigated NMII dysregulation in SSc skin using publicly available next-generation sequencing data. We then compared NMII expression,distribution, and activation in SSc vs. healthy donor (HD) fibroblasts resting or upon TGFβ stimulation. Immunofluorescence and western blotting assessed NMIIA, NMIIB, and myosin light chain (MLC) phosphorylation. Rho activity was measured using a pull-down assay. Pharmacological inhibitors targeting ROCK isoforms (Y-27632, KD025) and NMII (blebbistatin) along with NMIIB siRNA explored NMII role in fibrosis. Fibrotic markers production (IL-6, collagen I) was measured by ELISA and qPCR.

Results: In-silico analysis revealed an upregulated Rho-ROCK-NMII pathway in SSc skin. SSc-F displayed a distinct redistribution of NMII isoforms compared to HD, with increased NMII localization toward stress fibers ($p < 0.05$). TGFβ mimicked this effect in HDF ($p < 0.05$). These findings were validated through biochemical analysis of NMIIB distribution. Moreover, TGFβ stimulation increased Rho activation and MLC phosphorylation in HDF ($p < 0.01$). Importantly, inhibiting ROCK or NMII activity significantly blunted TGFβ-induced IL-6 and collagen I production ($p < 0.05$). Notably, ROCK2 inhibition specifically suppressed collagen production ($p < 0.05$). Similarly, NMIIB knockdown countered TGFβ profibrotic effects, decreasing collagen and IL-6 release ($p < 0.05$).

Conclusions: Our data unveil dysregulated NMII isoforms in SSc fibroblasts, highlighting their crucial role in TGFβ-mediated fibrogenesis. Targeting specific NMII isoforms or their upstream regulators holds promise as a therapeutic approach for SSc fibrosis.

Basic research 4

The protease HTRA1 generates pro-inflammatory extracellular matrix fragments in intervertebral discs with Modic type 1 changes

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Background: Vertebral bone marrow lesions, known as Modic type 1 (MC1) changes are inflammatory bone marrow changes that are highly specific for diskography concordant pain. Whilst MC1 are always adjacent to degenerated discs and damaged cartilage endplates (CEP), not all degenerated discs and damaged endplates have MC1. We hypothesized that MC1 discs release higher amounts of extracellular matrix (ECM) fragments during degeneration that can act as pro-inflammatory damage-associated molecular pattern (DAMP) by binding to toll-like receptor 2 (TLR2) or TLR4 on CEP cells.

Objective: To compare the 'degradome' of degenerated discs with and without MC1 and identify molecular mechanisms how the MC1 degradome can trigger inflammation.

Methods: Degenerated MC1 discs (n = 30) and degenerated non-Modic (nonMC) discs (n = 25) underwent N-terminal amine isotopic labelling of substrates (TAILS) and mass spectrometry to identify ECM-derived fragments and their abundance. The protease high-temperature requirement serine protease 1 (HTRA1) was assessed for its ability to generate the observed fragments from control discs (scoliotic discs, little degeneration). A NFκB reporter cell line and flow cytometry of phosphorylated NFκB were used to evaluate the pro-inflammatory potential of these fragments. Gene expression of TLR1-10 was compared in MC1 and nonMC cartilage endplate (CEP) cells. CEP destruction was measured after TLR2 activation by sulfated glycosaminoglycan (sGAG) release.

Results: TAILS revealed more fragments in MC1 disc of the ECM proteins fibronectin (FN), cartilage intermediate layer protein 1 (CILP1), and collagen alpha 1 chain (COL1A1). HTRA1 levels were higher in MC1 discs and HTRA1 was able to cleave FN, COMP, and CILP1 and to generate the same fragments from scoliotic control discs. CILP1 fragments produced by HTRA1 activated NFκB via TLR4. MC1 CEP cells exhibited higher TLR2 expression, suggesting prior DAMP exposure. TLR2 activation in CEP tissue led to upregulated inflammatory genes, matrix breakdown enzymes, and tissue destruction, as indicated by sGAG release.

Conclusion: HTRA1 may cause the observed accumulation of ECM fragments in MC1 discs. Fragments of CILP1 can trigger inflammation through TLRs. This is important because CEP cells express TLRs and their activation causes CEP degeneration, a hallmark of MC1. This results motivate to test inhibition of HTRA1 or TLR-pathways as a novel treatment option to for MC1.

Basic research 5

Low iron diet improves the course of clinical arthritis in the mouse model of collagen-induced arthritis

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Background: In chronic inflammatory conditions, the absorption of dietary iron is restricted. Since the pathophysiological significance of this iron restriction remains to be elucidated, we took advantage of the mouse model of collagen-induced arthritis (CIA) and assessed the effect of a low iron diet on the clinical arthritis course.

Methods: We fed six- to eight-week-old male DBA/1 mice with a normal (51 mg iron/kg) or a low (5 mg iron/kg) iron diet starting three weeks prior to arthritis induction (day 0). From day 25, we regularly monitored arthritis development and severity until the end of the experiment (day 34) by a standard clinical arthritis score. We measured complete blood count and Fe2+, Fe3+, oxidized/reduced glutathione and malondialdehyde as read-outs for oxidative stress and lipid peroxidation in whole paw tissue by ELISA. Key regulator genes of iron metabolism and ferroptosis, an iron-dependent mechanism of programmed cell death, were analyzed by quantitative PCR in whole paw tissue. Markers of iron metabolism and ferroptosis were compared by non-parametric tests. Nonlinear regression models were used for longitudinal data analysis of arthritis signs.

Results: Notably, mice fed a low iron diet had a significantly less severe course of arthritis in comparison to their counterparts fed a normal iron diet ($p < 0.001$). Low iron diet significantly reduced red blood cell lines, but did not affect hemoglobin. We could not find differences in Fe2+ or Fe3+ content, oxidative stress, which was high in both diet groups, and lipid peroxidation in the paws between the diet groups. We could not detect differences in gene expression of key regulators of iron metabolism and ferroptosis between the diet groups.

Conclusion: The restriction of dietary iron intake significantly alleviates the course of immune-mediated joint inflammation in CIA without causing anemia. From a translational perspective our data suggest that a hypoferric state in chronic inflammation should be understood as a biomarker of the body`s anti-inflammatory defense, which should not be counter-regulated, but therapeutically supported. Thus, a low iron diet appears as a promising tool for dietary treatment of arthritis. The underlying mechanism is most likely independent from local iron levels, oxidative stress, lipid peroxidation and ferroptosis, suggesting other, apparently extra-articular, mechanisms.

Basic research 6

Gamma-delta T cells modulate citrullinated autoreactivity development in HLA-DR4 transgenic mice exposed to cigarette smoke

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Background: Cigarette smoke (CS) has been associated with the production of anti-citrullinated protein antibodies (ACPAs) and an increased risk of developing ACPA+ rheumatoid arthritis (RA) in individuals carrying HLA-DRB1 risk alleles, of which DRB1*0401 (HLA-DR4) is the most described. However, the mechanisms that drive loss of tolerance and induction of T cell autoreactivity in response to CS are not fully understood. We hypothesized that innate-like T cells, such as γδ-T, can influence the local development of autoreactive T-cells against citrullinated peptides (cit-peptides) in the lungs of smokers.

Methods: To study in-vivo the interaction between CS and HLA-DR4 restricted T cell reactivity, we exposed HLA-DR4 transgenic mice for 4 (subacute) or 16 (chronic) weeks to air or CS. Innate-like T cells profiling was performed by mean of flow cytometry. MHC-II tetramer technology was used for detection of CD4+ T-cells with a T-cell receptor specific for 5 selected citrullinated peptides and for non-citrullinated Influenza Hemagglutinin peptide (HA) as control antigen. Cit-peptide immunization was performed to explore adaptive T cells responses.

Results: CS had a significant impact on lung residing T cell subsets: subacute CS-exposure led to a significant increase of γδ-T in lung environment. This effect was reinforced with chronic exposure, which also significantly increase γδ-T cells in mediastinal lymph nodes. Using HLA-DR4 tetramers loaded with cit-peptides, we demonstrated a significant increase in cit-peptide reactive CD4+ T cells in the lungs upon chronic CS exposure. Interestingly, we found a strong positive correlation between the numbers of lung residing cit-peptide reactive CD4+ T cells and γδ-T cells. No such effect was seen for control antigen (HA) tetra+ T cells. To further study the potential effect of γδ-T cells towards adaptive cit-peptide responses, HLA-DR4 and HLA-DR4 x TCRD-/- mice (lacking γδ-T cells) were immunized with cit-α-enolase. After in-vitro rechallenge of lymph node and splenic lymphocytes with cit-α-enolase, we observed a significantly reduced IFNγ & IL-17 responses in cultures from γδ-T deficient HLA-DR4 mice.

Conclusion: These data highlight the selective impact of CS on autoreactive and innate-like T cell subsets in the lung environment and suggest a modulatory effect of γδ-T cells towards HLA-DR4 mediated cit-peptide T cell responses, reflecting smoke-induced early immune changes prior to RA tolerance breakdown.

POSTERS SGR-SSR

P 1

Radioproteomics stratifies molecular response to antifibrotic treatment in pulmonary fibrosis

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Antifibrotic therapy with nintedanib is the clinical mainstay in the treatment of progressive fibrosing interstitial lung disease (ILD). High-dimensional medical image analysis, known as radiomics, provides quantitative insights into organ-scale pathophysiology, generating digital disease fingerprints. Here, we used an integrative analysis of radiomic and proteomic profiles (radioproteomics) to assess whether changes in radiomic signatures can stratify the degree of antifibrotic response to nintedanib in (experimental) fibrosing ILD. Unsupervised clustering of delta radiomic profiles revealed two distinct imaging phenotypes in mice treated with nintedanib, contrary to conventional densitometry readouts, which showed a more uniform response. Integrative analysis of delta radiomics and proteomics demonstrated that these phenotypes reflected different treatment response states, as further evidenced on transcriptional and cellular levels. Importantly, radioproteomics signatures paralleled disease- and drug related biological pathway activity with high specificity, including extracellular matrix (ECM) remodeling, cell cycle activity, wound healing, and metabolic activity. Evaluation of the preclinical molecular response-defining features, particularly those linked to ECM remodeling, in a cohort of nintedanib-treated fibrosing ILD patients, accurately stratified patients based on their extent of lung function decline. In conclusion, delta radiomics has great potential to serve as a non-invasive and readily accessible surrogate of molecular response phenotypes in fibrosing ILD. This could pave the way for personalized treatment strategies and improved patient outcomes.

P 2

Characteristics and disease course of systemic sclerosis patients with interstitial lung disease and gastroesophageal reflux disease – an analysis of the EUSTAR cohort

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Objectives: Gastroesophageal reflux disease (GERD) is frequent in systemic sclerosis (SSc) and could predict interstitial lung disease (ILD) progression. We aimed to analyse (1) the prevalence of GERD, (2) its association with disease characteristics and (3) the predictive factors for ILD progression in SSc-ILD patients with GERD.

Methods: SSc patients from the EUSTAR database with ILD on high-resolution computed tomography (HRCT) were included. GERD was labelled as present if reflux/dysphagia was reported at baseline visit or before. Baseline visit was set as first visit with ILD on HRCT. Disease characteristics of patients with and without GERD were compared at baseline. ILD progression was defined as relative FVC decline ≥ 10% or relative FVC decline between 5-9% in association with relative DLCO decline of ≥ 15% over 12±3 months of follow-up. Prognostic factors for ILD progression, overall survival and progression-free survival in SSc-ILD patients with GERD were tested by multivariate Cox regression.

Results: 5462 SSc-ILD patients were included, 4400 (80.6%) had GERD. Patients with GERD had a more severe disease with more frequently diffuse cutaneous SSc (OR: 1.44 [1.22-1.69], p <0.001), lower DLCO (OR: 0.99 [0.99-1.00], p = 0.015) and more use of ILD modifying treatments (OR 1.49 [1.25-1.78], p <0.001).

Female sex (HR: 1.39 [1.07-1.80], p = 0.012) and older age (HR: 1.02 [1.01-1.03], p < 0.001) independently predicted ILD progression in SSc-ILD patients with GERD. Use of PPI was associated with worse survival in the whole SSc-ILD population.

Conclusion: SSc-ILD GERD patients appear to suffer from a more severe disease form, particularly regarding lung involvement. Female sex may be considered as a risk factor for ILD progression in SSc-ILD patients with GERD.

P 3

Drivers of disease burden in patients with systemic sclerosis reported by the EULAR Systemic Sclerosis Impact of Disease (ScleroID) Questionnaire across clinical and demographic subgroups

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Introduction: A joint team of patients and physicians recently developed ScleroID as a novel patient-reported outcome measure (PROM) to capture disease burden of systemic sclerosis (SSc) (1). Herein, we aimed to investigate drivers of disease burden revealed by the ScleroID, to explore differences between demographic subgroups, correlations with other disease indices and longitudinal changes in relation to clinical disease progression.

Methods: The ScleroID cohort (1) included SSc patients from 9 European centers. We compared the ScleroID among different demographic groups, disease manifestations, and analyzed correlations with patient's and physician's global assessment of disease activity (PtGA, PhGA) and self-perceived changes in disease activity at baseline and 1-year follow-up. We used the Spearman correlation- and Wilcoxon rank sum or Kruskal-Wallis tests for the analysis, which was performed in R.

Results: We included 471 patients (median age 57 years, 84.7% female, 62% limited cutaneous SSc). Significantly higher ScleroID scores were observed in retired and medically disabled patients, lower educated patients, women, disease duration >5 years, digital ulcers, severe dyspnea, ILD, and esophageal symptoms. Interestingly, not only the corresponding ScleroID health dimension, but also multiple others, were affected. The ScleroID score strongly correlated with PtGA ($\rho = 0.78$, $p < 0.001$) but weakly with PhGA ($\rho = 0.29$, $p < 0.001$). There was a weak correlation between ScleroID and the European Scleroderma Study Group activity index ($\rho = 0.23$, $p < 0.001$). Patients with clinical disease progression (n = 9) had significantly higher changes in ScleroID scores ($p = 0.03$), though only 5/9 self-reported worsening.

Conclusion: Disease duration >5 years, female sex, digital ulcers, severe dyspnea, ILD and esophageal reflux, as well as work disability and a lower education status, were important drivers of a high disease burden as reflected by higher ScleroID scores. At follow-up, we found higher changes in ScleroID scores among patients with clinical disease progression, which was only partially recognized by the patients themselves. This aspect, together with the discrepancies between the PtGA and PhGA, emphasize the need for integrating PROMs in the regular monitoring for clinical care and research.

1. Becker MO, Dobrota R et al Development and validation of a patient-reported outcome measure for systemic sclerosis: the EULAR Systemic Sclerosis (ScleroID) questionnaire Ann Rheum Dis 2022

P 4

Immunosuppression versus combination of immunosuppression and oral glucocorticoids for skin fibrosis in early diffuse systemic sclerosis patients. A target trial emulation study from the EUSTAR database.

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Objectives. To evaluate if adding oral glucocorticoids to immunosuppression improves skin score and is safe in patients with early diffuse cutaneous systemic sclerosis (dcSSc).

Methods. We performed an emulated randomized trial comparing the changes from baseline to 12 ± 3 months of the modified Rodnan skin score (mRSS: primary outcome) in early dcSSc patients receiving either oral glucocorticoids (< 20 mg/day prednisone-equivalent) combined with immunosuppression (treated), or immunosuppression alone (controls), using data from the European Scleroderma Trials and Research Group. Secondary endpoints were the difference occurrence of progressive skin or lung fibrosis, and scleroderma renal crisis. Matching propensity score was used to adjust for baseline imbalance between groups.

Results. We matched 208 patients (age 49 years; 33% male; 59% anti-Scl70), 104 in each treatment group, obtaining comparable characteristics at baseline. In the treated group, patients received a median prednisone dose of 5 mg/day. Mean mRSS change at 12 ± 3 months was similar in the two groups (decrease of 2.7 [95% CI 1.4–4.0] in treated vs. 3.1 [95% CI 1.9–4.4] in control, $p = 0.64$). Similar results were observed in patients with shorter disease duration (≤24 months) or with mRSS ≤22. There was no between-group difference for all prespecified secondary outcomes. A case of scleroderma renal crisis occurred in both groups.

Conclusions. We did not find any significant benefit of adding low-dose oral glucocorticoids to immunosuppression for skin

fibrosis, and at this dosage, glucocorticoid did not increase the risk of scleroderma renal crisis.

P 5

Low expression of CD169 on urine monocytes inversely correlates with CD169 expression on blood monocytes and indicates severity of renal involvement in SLE patients

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Background: Nephritis represents one of the clinically most relevant organ manifestations of systemic lupus erythematosus. Expression of CD169 (SIGLEC1) on peripheral blood monocytes has been proposed as a surrogate for increased disease activity.

Objectives: To study CD169 expression on urine and peripheral blood monocytes in SLE patients in correlation to clinical characteristics and serological markers of disease activity.

Methods: 64 patients enrolled in the Swiss SLE Cohort Study (SSCS), were consecutively recruited into this prospective cross-sectional, observational study. Expression of CD169 on urine and blood monocytes was assessed using quantitative flow cytometry.

Results: 37.5% of SLE patients had active disease with a SELENA-SLEDAI = / >4 and 14/64 (22%) of SLE patients had biopsy proven lupus nephritis class III-V. Expression of CD169 on blood monocytes in SLE patients was significantly higher compared to age and sex matched HC (p = 0.0016) while it was significantly lower on urine monocytes. In SLE patients, CD169 expression on peripheral blood, but not urine, monocytes positively correlated with disease activity (SELENA-SLEDAI) (r = 0.384, p = 0.002), ESR (r = 0.341, p = 0.006), and anti-dsDNA abs levels (r = 0.513, p <0.0001), while an inverse correlation was observed with C3c (r = –0.290, p = 0.021) levels. Moreover, biopsy proven renal manifestation (r = 0.419, p = 0.001), fever (r = 0.551, p <0.0001), rash (r = 0.322, p = 0.01), and leucopenia (r = 0.334, p = 0.007) were associated with expression of CD169 on blood monocytes. A decreased CD169 expression on urine monocytes (<20%) was detected in 67% of all SLE patients, of note in all 14 patients with biopsy proven nephritis, and in 38% of HC (p = 0.0006). A lower CD169 expression on urine monocytes was associated with an increase in SELENA-SLEDAI (r = 0.280, p = 0.026), with biopsy proven renal manifestation (r = 0.262, p = 0.038), an increased albumin/creatinine ratio (r = 0,351 p = 0.005) and with serum creatinine levels (r = -0.331, p = 0.008), the presence of anti-Sm- (r = 0,457 , p <0.0001) and levels of anti-dsDNA- (r = 0,290 , p = 0.021) abs.

Conclusion: In this cohort, higher expression of CD169 on blood monocytes inversely correlated with decreased CD169 expression on monocytes in urine (r = 0.336, p = 0.007), and was associated with the presence of renal disease and markers of active renal SLE disease. Our data suggest that lower CD169 expression on monocytes in urine than on monocytes in peripheral blood indicates more severe renal involvement.

P 6

Elevated serum levels of IL-18 discriminate Still's Disease from other autoinflammatory conditions: results from a unique European cohort

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Background: Autoinflammatory diseases (AIDs) pose diagnostic challenges due to their rarity and severity. IL-1β and IL-18 (a strong IFN-γ inducer) are pro-inflammatory cytokines of the IL-1 family that are secreted upon inflammasome/caspase pathway activation, and already represent relevant therapeutic targets in some AIDs.

Aim: We aimed to measure the serum levels of IL-1β, IL-18 (including in its bioactive, IL-18 binding protein (IL-18BP)-unbound form), their respective inhibitors IL-1Ra and IL-18BP, and IFN-γ in a large European cohort of AID patients (ImmunAID consortium).

Methods: Adult and pediatric patients with monogenic or genetically undiagnosed AIDs from 34 centers, with active disease according to predefined criteria, were enrolled for serum and clinical data collection. Individuals without inflammatory conditions were selected as controls. Commercial ELISAs were used to measure IL-18, IL-18BP, IL-1Ra and IFN-γ, while free IL-18 levels were quantified using a homemade ELISA. IL-1β levels were assessed using an electrochemiluminescence assay. Levels of cytokines and their inhibitors were compared between diseases themselves and between each disease and healthy controls. Correlations were established between cytokine levels and reported clinical (e.g. maximal body temperature, disease activity score) and laboratory data (e.g. CRP, ferritin, serum amyloid A). ROC curves were drawn to assess the diagnostic value of various parameters.

Results: Two hundred and seventy-three patients and 49 negative controls were included. Adult and pediatric Still's disease was the most represented AID (61 patients), followed by inflammation of unknown origin (IUO) (47), chronic/recurrent osteomyelitis (33) and familial mediterranean fever (31). Total IL-18 and free IL-18 were higher in Still's disease than in other AIDs. IFN-γ was significantly higher than in controls only in Still's disease, IUO and mevalonate kinase deficiency. IFN-γ levels correlated with total and free IL-18 (r = 0.37 and 0.30 respectively, p <0.0001). In contrast, IL-1β, IL-1Ra and IL-18BP levels did not frankly differ between AIDs patients. Total and free IL-18 correlated strongly with ferritin (r = 0.44 and 0.52 respectively, p <0.0001) and served as promising predictors of Still's disease (AUC: 0.92 and 0.85, respectively).

Conclusion: Our findings highlight the diagnostic potential of IL-18 in Still's disease and support targeting the IL-18-IFN-γ axis in its management.

P 7

Hemophagocytic lymphohistiocytosis in the context of systemic lupus erythematosus and HHV8-reactivation

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Background: Secondary hemophagocytic lymphohistiocytosis (HLH) is a life-threatening, highly inflammatory disorder, triggered by infections, malignancies or autoimmune diseases.

Case presentation: A 24-year-old male patient, who migrated to Europe from Burundi two years before, was diagnosed at our

hospital with SLE due to elevated anti-DNA/Nucleosome/C1q-Antibodies, low complement protein C3, acute mucocutaneous manifestations, pancytopenia, pericardial effusion and a class II lupus nephritis.

Eight months after the diagnosis the patient presented with treatment-related lymphopenia (0.6 G/l), on azathioprine and hydroxychloroquine, developed significant pancytopenia and high fever. Elevation of CRP (80mg/l), ferritin (9776 µg/L), transaminases, and particularly, sIL-2R occurred. Raising C3 and dropping anti- ds-DNA titers indicated control of SLE activity. Thus, based on an HLH score of 267 points, secondary HLH was diagnosed, triggered by a pronounced reactivation of human herpes virus 8 (HHV8). Other differential diagnosis, particularly, HIV-infection, Castleman disease, and HHV8-related Kaposi sarcoma were ruled out including panendoscopy. High-dose IV glucocorticoids and the IL-1R-inhibitor anakinra were started. In a refractory situation with hyperfibrinolysis, IV immunoglobulins were added, and a further escalation with the JAK-inihibitor ruxolitinib was planned. Shortly after gastroscopy, the patient developed a severe retroperitoneal hematoma with hemorrhagic shock, likely due to an arterial injury. After recuperation, a generalized seizure occurred. Invasive cerebral and pulmonary aspergillosis was diagnosed and voriconazole started. After resolution of a paralytic ileus ruxolitinib 10 mg/day (reduced dose due to interaction with voriconazole) was finally started and the patient gradually improved. Two months after discharge, corticosteroid-free clinical remission was achieved under ruxolitinib and hydroxychloroquine for both, SLE and sHLH.

Learning points for clinical practice

sHLH needs to be included in the differential diagnosis of cytopenia in SLE.

Viral reactivation is a common trigger of HLH in immunodeficient patients.

The JAK inhibitor ruxolitinib is a viable treatment option in adult patients with (virus-induced) sHLH and SLE.

P 8

Oculomotor nerve palsy as atypical presentation of giant cell arteritis

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Microvascular ischemia is generally regarded as the most common cause of isolated ocular motor nerve palsy in elderly patients. Giant cell arteritis (GCA) is among the possible etiologies. We here report on two patients in whom oculomotor nerve palsy was the initial symptom of cranial GCA.

A 74-year-old patient presented in the neurology department because of a new-onset vertical diplopia. As a cranial MRI excluded cerebral ischemia, the patient was transferred to the ophthalmologists, who confirmed a diagnosis of right-sided complete oculomotor palsy. In addition, the patient reported pain on mastication and rightsided temporal headache. Laboratory analyses revealed elevated an elevated ESR and CRP. Temporal artery ultrasound and CSF analysis were normal. However, a contrast dark-blood MRI of the extracranial arteries revealed a slight enhancement of the temporal artery walls that was considered suspicious for GCA. Prednisolone was started and complete resolution of symptoms occurred within weeks.

A 71-year-old male was referred to the neurology department because of a right-sided incomplete oculomotor nerve palsy with lateral and downward gaze deviation. We noted a tender right temporal artery and slightly elevated inflammatory parameters. Temporal artery ultrasound and CSF analysis were normal. A cranial dark-blood MRI revealed a slight enhancement of the right temporal artery wall. Temporal artery biopsy was performed and confirmed GCA. Prednisolon was started and resulted in rapid resolution of the oculomotor nerve palsy.

In summary, these two cases demonstrate that among potential ophthalmic features, GCA may not only present with typical complications like anterior ischemic optic neuropathy, but may atypically present with diplopia resulting from the involvement of the third cranial nerve.

P 9

Unusual cause of inflammatory back pain in a 26-year old male

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A 26-year-old Patient presented with non-traumatic lumbar and right paralumbar pain for 4 months without radicular pain. The pain appeared when he was bending over or after sitting or standing for a while. While laying down he sometimes struggled to find a comfortable position, but when he did the pain faded away completely. There was no nocturnal awakening, no sensorimotor deficits, no bladder or rectal dysfunction. Also no B-symptoms. Occasional intake of paracetamol or NSAIDs lead to complete pain remission. Physiotherapy had not yet been established.

On clinical examination the patient appeared healthy, with no abnormalities in posture or allignement of the spine. Percussion over the lower lumbar spine was severely painful, and exquisite tender points of the right paraspinal and quadratus lumborum muscles were present. While laying down there was pain on palpation located over facet joints and multifidi muscles at LWK 3-LWK 5 level with pain recognition. Furthermore, flexion, extension and lateral flexion to the left of the lumbar spine were all painful.

Treatment was started with physiotherapy without any positive effect. He started avoiding any kind of sports by fear of triggering the pain. After a second set of physio without any improvement, we performed an MRI, which showed extensive edematous changes in the right dorsal part of the fourth lumbar vertebra extending via the right pedicle into the right superior articular process, the right and left lamina and the multifidus muscle over lumbar segments three and four. The suspected diagnosis was corroborated by CT scanning of the spine, and the patient was referred to spinal surgery. The final diagnosis and successful treatment of the patient will be discussed.

P 10

Not every pretibial nodule it's erythema nodosum

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Introduction: Gout is a very prevalent disease. Inadequate disease control can lead to the formation of tophi, the most common locations being synovium, subchondral bone, digits, olecranon bursa and Achilles-tendon.

The case: In 2022, a 47-year-old man who had from liver cirrhosis, diabetes, alcoholic polyneuropathy complicated by Charcot foot and gout since 15 years was referred to our clinic. Allopurinol was started (preferred over Febuxostat due to cirrhosis), then replaced colchicine because of dizziness. The

later was also discontinued due diarrhea. Early in 2023, the patient experienced several flares in the left elbow and ankle, treated with a short course of Anakinra and joint infiltrations with good results. The assessment of foot pain was challenging due to the concurrent presence of Charcot's foot. Suspecting a poor control of gout disease and having few therapeutic options, we did several trials with low dose febuxostat and benzbromarone but stopped the drugs due to side. Disease relapses bursitis of the left elbow were treated with short courses of prednisone. A differential diagnosis of sarcoidosis was considered in August 2023 because pulmonary micronodules were detected on CT scan, in the presence of reddish, inflammatory small nodules on the skin of the lower legs, suggesting an erythema nodosum, as well as ankle swelling. Following laboratory tests were normal: ACE, IL-2R, calciuria, calcemia, phosphate, active vitamin D. At the follow-up visit in December 2023 the patient was re-evaluated. Clinical and echographical examination confirmed the presence of numerous hard subcutaneous nodules of 3 mm without erythema ("grains of rice"-like), opening the differential diagnosis of tophi. The urate was elevated (449 umol/L) and the ESR was 40 mm/h. A skin biopsy on the left pretibial region performed by dermatologists in January 2024 confirmed the diagnosis. At the same time, a pulmonary sarcoidosis was ruled out after additional pulmonary investigations. Finally, based on the clinical, laboratory-, and specialist's evaluation we concluded that the most likely diagnosis was a refractory tophaceous gout with cutaneous tophi. Unsurprisingly the hyperuricemia persisted (537 umol/l in May 2024), and we treated the last gout flare with Canakinumab 150 mg s.c.

Conclusion: This case highlights the need of awareness of the diverse clinical manifestations of tophaceous gout and illustrates treatment difficulties.

P 11

The solution lies where the eye falls

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A 47-year-old female patient presented in 2022 with arthritis of the proximal interphalangeal joint (PIP) III of the left hand. Systemic evaluation of patients symptoms were negative for signs of connective tissue disease or spondyloarthritis, but HIV and hepatitis B were known pre-existing conditions. Clinical examination revealed no other painful or swollen joints and no signs of enthesitis. Laboratory examination showed no signs of systemic inflammation (normal CRP, BSR) and normal values for rheumatoid factor and anti-CCP antibodies as well as unremarkable ANA titers. Radiologically, there were no bony changes visible. Therapeutically, an infiltration of the inflamed PIP III with 10mg Kenacort was performed. After initial improvement, arthritis recurred after a few months in the same joint and in addition in the PIP joint III of the right hand. In the absence of disease control, further diagnostics were performed using ultrasound-guided synovial biopsy. Surprisingly, gout tophi were found in the formalin-fixed tissue in histology. Further assessment of the hands with dual-energy CT showed no urate crystals within the joint but in the surrounding soft tissue, reinforcing the diagnosis of gout.

Discussion: Synovial biopsies are performed for further diagnosis of undifferentiated arthritis in the absence of clarification from previous examinations such as laboratory, imaging and punctate analysis. Ultrasound-guided synovial biopsy is well tolerated by patients, inexpensive, less invasive and can be used for small and large joints. The side effects are mild, transient and rare (approx. 0.5%). Standardized processing of the samples includes microbiologic assessment including Gram staining, culture and PCR testing for potential pathogens; histology and immunohistochemistry to classify the inflammation based on the most prevalent cells (e.g. synovial pathotypes) and observation for possible crystal depositions. In our case, synovial biopsy was able to lead to the right diagnosis in a case of undifferentiated arthritis. In gout, the gold standard for diagnosis remains puncture analysis with the presence of uric acid crystals or visible tophi within the fluid. However, puncture – as in our case – is not always possible. Ultrasound-guided synovial biopsy represents a possible alternative diagnostic path. In our case, puncture analysis was not possible in the absence of joint effusion.

P 12

When Rheumatoid Arthritis climbs to the head.

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A 91 years old woman was diagnosed with seropositive rheumatoid arthritis (RF, ACPA +) in 2021 and treated with methotrexate 10mg/we sc. Shee has a medical story of chronic kidney disease KDIGO 3, related to angiosclerosis,. In April, she presents a transient loss of strength in the right upper limb. Upon admission, the RA appears in remission with no tender nor swollen joint. The neurological examination is strictly normal. A transient ischemic attack is suspected and an MRI excludes a haemorrhagic or ischemic stroke but reveals a pachyleptomeningitis in the right frontoparietal region. An EEG confirms slowing in the right hemisphere without formal epileptic activity. A few days later, the patient develops a transient left-sided hemiparesis. Biological tests don't find increased inflammatory markers; autoantibodies show slightly positive RF and ANA 1/160 (mitotic aspect). ANCA, Anti-ENA, Anti-neuronal, and anti-surface receptor antibodies are negative. A lumbar puncture shows elevated protein levels (884mg/L) without intrathecal immunoglobulin secretion and a sterile culture. Clinical evolution and CSF analyses exclude bacterial or viral meningitis. Serologies are negative. Neoplastic cells in the CSF were alse negative. Therefore, a carcinomatous origin seems less possible. A vasculitic origin seems unlikely. Patient shows favourable evolution without specific treatment and is discharged. 48 hours later, the patient is readmitted due to altered consciousness, worsening left-sided hemiparesis and sudden onset aphasia. MRI shows no changes, pachymeningitis aspect remains unchanged. Another lumbar puncture is performed, testing for RF, ACPA, IL-6, and CXCL-13 in the CSF, suspecting rheumatoid pachymeningitis. The patient refuses a brain biopsy. IL-6 determination turns positive (421 pg/mL) in CSF reinforcing the idea of an inflammatory origin. Methylprednisolone treatment is initiated, resulting in clinical stability with no new symptoms but a better conscious state. A rituximab treatment is planned with an MRI at 1 and 6 for follow up and treatment adjustment. Rheumatoid meningitis is a rare extra-articular manifestation. It can occur at any moment of the disease. Symptoms are non-specific, mimicking other neurological diseases, infections or malgnancies. It should be suspected in cases of unifocal leptomeningitis or pachymeningitis. Diagnosis remains challenging and is still based on brain histology.

P 13

Severe Systemic Sclerosis Treated with Autologous Hematopoietic Stem Cell Transplantation

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Background: In severe, refractory diffuse cutaneous systemic sclerosis (dcSSc), autologous hematopoietic stem cell transplantation (aHSCT) represents a life-saving and potentially curative therapeutic option.

Case presentation: We report two cases of patients with dcSSc with life-threatening 1) lung and 2) cardiac involvement, who were rapidly progressive and refractory to extended pharmacological treatment including cyclophosphamide. Both underwent aHSCT in 2023 following the UPSIDE Study-Protocol (Spierings J et al. BMJ Open. 2021 Mar 18; 11(3):e044483. doi: 10.1136/bmjopen-2020-044483). AHSCT was well tolerated in both patients (aplasia of 8 resp. 9 days).

Case 1: A 49-year old man presented with Raynaud's phenomenon (RP), diffuse skin fibrosis (mRSS 13/51), synovitis, progressive ILD (NSIP, mean total disease extent (MTDE) 42%, Pulmonary Function Tests (PFT) with TLC of 4.08 l (59%), FVC of 2.87 l (60%), DLCO of 34% and incipient pulmonary arterial hypertension (right heartcatheterization). The 3- and 6-months follow-up showed a stable, respectively decreased ILD extent and decreased skin fibrosis (mRSS 10/51). Anti-Scl70 titers dropped from >240 to 157 and 137 U/ml respectively. PFT improved to TLC 4.40 l (63%), FVC 3.25 l (68%) and TLC 4.21 l (61%), FVC 3.73 l (75%). DLCO increased to 47% and 54% respectively.

Case 2: A 40-year old man presented with RP with active pattern on nailfold capillaroscopy (NVC), digital ulcers, diffuse skin fibrosis (mRSS 19/51), synovitis (CRP 12 mg/L), myositis, diffuse myocarditis/myocardial fibrosis (ECV, T1, T2 on cardiac MRI,elevated troponin I; LVEF 70%), and ILD (NSIP pattern; MTDE 16% on HRCT; PFT with TLC of 5.8 l (79%), FVC of 4.37 l (81%), DLCO of 66%. At 3- and 6-months follow-up, mRSS was decreased to 12/51 and 10/51 respectively, NVC changes were normalized and synovitis was absent at month 3. cMRI showed normalization with only minimal late gadolinium enhancement at month 3. Troponin I and CRP levels decreased to normal at month 3. Anti-Scl70 titers fell from >240 to 61 U/ml and 58 respectively. MTDE on HRCT at month 3 and 6 was stable with 17%. PFT at month 3 improved to TLC 6.03 l (82%), FVC 4.69 l (87%) and DLCO to 76% (PFT at month 6 not useable because of in-compliance).

Learning points: If provided by interdisciplinary teams with expertise in SSc and cellular therapies, aHSCT is a safe and excellent treatment option for selected patients with dcSSc, particularly with risk factors for progressive disease.

P 15

A feedback loop involving mtDNA, platelets and neutrophil extracellular traps amplifies inflammation in systemic sclerosis

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Mitochondria are essential eucaryotic cell organelles with several bacterial features such as a double-stranded circular genome with hypomethylated CpG area. A fundamental role of mitochondria in autoimmunity was recently demonstrated. In brief, mitochondrial ROS participate in the formation of neutrophil extracellular traps (NETs, while extrusion of cell-free mitochondria and highly oxidised interferogenic mitochondrial DNA (ox-mtDNA) causes autoimmune disease in an animal model. In other connective tissue diseases, plasma mtDNA is a diagnostic biomarker, also reliable in the monitoring of disease activity, while platelets might also contribute as a major source of circulatory mtDNA.

The present study aimed to explore the cellular mechanisms controlling the inflammatory responses triggered by mtDNA in systemic sclerosis (SSc).

Total DNA was isolated from plasma samples of healthy individuals and SSc patients. Copy numbers were analysed for mitochondrial (mt) DNA (ATP-6) and nuclear (n) DNA (GAPDH) abundance by qPCR. mtDNA was isolated from HC and SSc patients. Patients were stratified based on mtDNA levels. Neutrophils and platelets were isolated from EDTA and citrate blood respectively; cells were incubated with SSc patients' plasma and mtDNA, and NET formation was assessed by SytoxGreen staining. Platelets were tested for mtDNA release propensity. DNA oxidation was evaluated by MitoSOX Red staining in vitro and 8-OHdG ELISA of patient plasma. Plasma IFN type 1 was measured by ELISA. Platelet activation was assessed by IF staining in vitro and ELISA for CXCL4.

SSc patients' plasma contains elevated levels of highly oxidized mtDNA. Healthy donors' blood neutrophils incubated with plasma from patients with SLE exert enhanced NET formation, and NETs are decorated with oxidised mtDNA. SSc patients' peripheral blood is characterized by vigorous augmented type I IFN-stimulated gene transcripts. Furthermore, SSc platelets contain and release oxidized mtDNA, eliciting increased NET formation and mtDNA release from activated platelets. Moreover, mtDNA amounts correlate with CXCL4 and type I IFN levels in SSc patients' plasma. Finally, formation of NETs and ox-mtDNA extrusion are conveyed through the type I IFN pathway.

SSc plasma is characterized by an abundance of mtDNA that promotes positive feedback loops driving its release by NETs and platelets. Moreover, mtDNA is particularly interferogenic and may contribute to tissue damage and fibrosis in SSc.

P 16

A Novel 3D-Synovium-Immune Microenvironment Mimics Macrophage-Synovial Fibroblast Interactions in Inflammatory Arthropathies

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Trauma, autoimmunity or infection lead to devastating arthropathies, with enormous socioeconomic impact. The development of novel treatments remains a significant clinical challenge. Moreover, disease aetiology, sequence and drug responsiveness are exceptionally patient-specific, underscoring the need for personalised therapeutic strategies. In vitro cultures and animal models have been helpful in identifying and describing the pathological processes in arthritis; still, they cannot predict individual responses to treatment.

We sought to establish a credible and reproducible cutting-edge organoid model that emulates the complex biological interactions within the human synovium and pathological conditions of the inflamed joint.

For establishment of 2D and 3D cell cultures, native synovial fibroblasts and THP1 macrophages were utilised. Organoids were assembled by adding biocompatible magnetic nanoshuttles and subsequent bioprinting, allowing self-assembly of cells into 3D structures by building autologous ECM. This supports a native microenvironment preserving endogenous tissue phenotypes. Optimal setup parameters and culture were further tested.

The feasibility of the organoids to exhibit inflammatory responses in the presence of disease-relevant stimuli was assessed by measuring the secretion of RA-associated cytokine patterns (ELISA) and the expression of cellular phenotypes (IHC).

Biological material was collected and stored. This led to successful establishment of 2D and 3D in vitro synovial fibroblast and THP1 macrophage cultures, cocultures and organoids. Macrophage incorporation in the synovial organoid was confirmed in different coculture schemes. Data from a restricted set of RA-relevant markers displayed a synergistic effect coculture settings on proinflammatory cytokine secretion after distinct stimulation. Moreover, initial assessments comparing the 2D cultures and 3D organoids upon inflammatory stimulation showed that macrophages are the main source of TNFα.

Establishment of an engineered human 3D synovial tissue model, physiologically analogous to the human synovium by utilizing targeted tissue material, serves to functionally test essential aspects of synovial inflammation. The ability to induce inflammatory responses provides a proof of concept for cytokine-driven inflammation in autoimmunity. This will substantially improve the drug development process and tackle the limited predictive value of existing in vitro and in vivo animal models.

P 17

Lysyl oxidase (LOX) and lysyl oxidase-like 2 (LOXL2) contribute to cartilage calcification during osteoarthritis

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Background: Cartilage pathologic calcification (PC), characterized by the deposition of calcium-containing crystals, is a pivotal feature in osteoarthritis (OA). We previously showed that lysyl oxidases (LOX(L)) play a major role in PC as their inhibition decreased in vitro and in vivo crystal production.

Objective: We want to establish the specific LOX(L) involved in PC during OA and the underlying mechanisms.

Methods: In vitro, murine (mCHS) and human chondrocytes (hCHS) from 5 OA patients as well as human chondrocyte cell line TC28 were cultured in calcification medium (CM). hCHS were treated or not with LOX(L) inhibitor BAPN. CM-stimulated TC28 and mCHS were silenced for LOX and LOXL2 (siRNA). Ex vivo, undamaged and damaged cartilage explants were obtained from 7 OA patients. In vivo, OA was induced in mice by menisectomy (MNX) in the right knee while the left was sham-operated. Calcification was evaluated in vitro by Alizarin Red, in vivo by µCT scan; proteoglycan loss by Safranin-O; gene expression by RTqPCR; LOX and LOXL2 production by immunohistochemistry; and interleukin 6 (IL6) secretion by ELISA.

Results: We identified that Lox and Loxl2 were the most expressed Lox(l) in mCHS. When stimulated with CM, Lox expression was increased. In addition, we observed increased LOX and LOXL2 in MNX cartilage, with even higher production in osteophytes and in newly formed calcified deposits compared to sham cartilage. In human explants, massive calcification and proteoglycan loss was found in damaged compared to undamaged cartilages. We also revealed increased LOX and LOXL2 production in damaged cartilage, both in chondrocytes and in the extracellular matrix in correspondence to calcified regions. Next, we analyzed siLOX and siLOXL2 effects on chondrocytes. In both conditions, calcification deposition and IL6 secretion were markedly reduced. No modulation of catabolic nor hypertrophic genes was observed. However, in siLOX condition, ENPP1 expression (known to generate pyrophosphate, inhibitor of calcification) was significantly increased. Interestingly, LOX(L) inhibition in hCHS also showed decreased calcification accompanied by ENPP1 upregulation.

Conclusion: Our data revealed that LOX and LOXL2 are increased in calcified areas of cartilage. Their specific inhibition prevents calcification deposition and inflammation, suggesting their potential role in cartilage calcification and OA. Further studies are ongoing to decipher the LOX-ENPP1 axis in calcification.

P 18

Inflammatory gene enhancers are shared in synovial fibroblasts and minor salivary gland fibroblasts

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Background: Cell type- and stimulus-specific enhancers are key regulatory elements in chronic inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) and Sjögren's disease (SjD). Enhancer RNAs (eRNAs) are short-lived non-coding RNAs transcribed from cell type-specific enhancers that facilitate the transcription of their linked coding genes.

Objectives: To characterise the activation and regulation of transcribed inflammatory gene enhancers in fibroblasts from synovium (FLS) and salivary glands (SGF).

Methods: FLSwere isolated from synovial tissues of patients with RA undergoing joint replacement surgery. SGF were isolated from minor salivary gland (MSG) biopsies of patients with a suspected SjD. The expression of TNF-induced eRNAs in FLS was detected by cap analysis of gene expression followed by sequencing (CAGEseq). RA FLS (n = 7) and SGF (n = 6) were stimulated with TNF, IL1, or the Toll-like receptor agonists poly(I:C) and LPS in absence and presence of the bromodomain inhibitor I-BET (1 µM). The expression of eRNAs and coding genes in FLS, SGF and MSG tissues was analysed by real-time PCR.

Results: We have identified and selected a set of TNF-induced eRNAs for the pro-inflammatory genes CCL2, IL8, IL6, CXCL1 and CCL20 for a more detailed analysis. These eRNAs were located upstream, downstream and intronic at distances between 300 bp to 35.6 kb relative to the transcription start sites of the corresponding coding genes. We have detected different patterns of eRNAs: (a) eRNAs, that peaked at 1h (eCCL20, eIL8#2, eCCL2#1), (b) at 6h (eCXCL1#1), (c) or at 24h (eIL8#1, eIL8#3, eIL8#4, eCXCL1#2) after stimulation, and (d) eRNAs that were stably expressed over the time points (eCCL2#2, 3, 4). Treatment of FLS with I-BET suppressed the expression of all eRNAs tested. The same set of eRNAs and corresponding coding genes was induced in SGF, indicating that inflammatory gene enhancers are shared in fibroblasts from different localisation and diseases. Furthermore, we detected eIL6 and eIL8#3 in MSG tissues, where their expression correlated with the expression of the corresponding coding genes.

Conclusions: SGF, similar to FLS, respond to different pro-inflammatory stimuli by inducing the expression of transcribed eRNAs and their corresponding coding genes. Bromodomain inhibitors are sufficient to prevent the activation of eRNAs. The measurement of eRNAs in tissues may provide information on the cellular source of expressed cytokines and chemokines.

P 19

Ankylosing spondylitis patients present a distinct CD8 T-cell subset with osteogenic and cytotoxic potential

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Background: Ankylosing Spondylitis (AS) is a chronic inflammatory rheumatic disease mainly affecting the axial skeleton. AS is responsible for chronic and severe back pain caused by local inflammation that can lead to osteoproliferation and to spinal fusion. Peripheral involvement (arthritis, enthesitis, and dactylitis) and extra-musculoskeletal manifestations including uveitis, psoriasis and bowel inflammation also occur in a significant proportion of patients. The chemokine system finely regulates leukocytes recruitment at sites of inflammation. Previous reports highlighted elevated levels of CCL17 and CCL22, ligands of the chemokine receptor CCR4, in the sera of patients with AS.

Objective: This study aims to investigate the role of CD8+CCR4+ T-cells in the disease pathogenesis.

Methods CD8+CCR4+ T-cells isolated from blood of AS patients (n = 76) or healthy donors were analysed by multi-parameter flow cytometry and gene expression evaluated by RNA sequencing. AS patients were stratified according to the therapeutic regimen and disease score at time of enrolment.

Results: CD8+ CCR4+ T-cells display a distinct effector phenotype and upregulate the chemokine receptors CCR1, CCR5, CX3CR1 and the L-selectin CD62L, suggesting their ability to migrate to inflamed tissues. In addition, CD8+CCR4+ T-cells expressing CX3CR1 present an enhanced cytotoxic profile, expressing both perforin and granzyme B. Of note, CD8+CCR4+ T-cells, isolated from patients in the active state of the disease, upregulate genes promoting the ossification process.

Conclusions: Our results shed light on a subset of T-cells that, due to their chemokine receptors expression profile, may selectively migrate to sites of inflammation. Locally, these cells could induce tissue damage, thus sustaining inflammation, and promote new bone formation, contributing to the pathological ossification process observed in AS.

P 20

Bone marrow adipose tissue-mediated lipolysis regulates aberrant bone formation in hand Osteoarthritis

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Purpose: Bone marrow adipose tissue (BMAT) and adipocytes (BMAds) are emerging as regulators of bone formation by releasing free fatty acids and glycerol through lipolysis. However, the influence of BMAT on subchondral bone remodeling in osteoarthritis (OA) remains unclear. This study aims to explore the association between BMAT lipolysis and bone remodeling in hand OA.

Methods: Resection specimens were collected from patients with base of the thumb (CMC1, n = 20, 13 female) or distal interphalangeal OA (n = 4, 2 female) undergoing joint replacement. Average age and BMI were 66 ± 10 years and 25.5 ± 5.5

kg/m2. Specimens were processed for histology (n = 13) or explant culture (n = 11). Bone markers (ALP, pro-collagen-Iα) and BMAd-derived factors (free fatty acids, glycerol) were measured in supernatant. BMAd size and osteoblasts were quantified in ROIs displaying low or high subchondral bone (sclerosis) and BMAT remodeling. Expression of adipose triglyceride lipase (ATGL), phosphorylated hormone-sensitive lipase (p-HSL) and monoacylglycerol lipase (MGLL) was assessed by immunohistochemistry.

Results: BMAd size was associated with BMI in low remodeling ROIs. In sclerotic ROIs, BMAd size was reduced and osteoblast numbers were increased. Relative changes in BMAd size and osteoblast numbers were correlated. Sclerotic ROIs displayed increased expression of lipolysis enzymes ATGL (1.7-fold), p-HSL (2-fold) and MGLL (2.9-fold) in both BMAd and bone-lining cells. Bone formation markers pro-collagen-Iα (r = 0.90) and ALP (r = 0.76) were correlated with secreted glycerol levels.

Conclusions: These findings suggest that BMAT plays a role in hand OA through increased lipolysis contributing to bone remodeling and potentially regulating OA progression. BMAd properties in non-weight-bearing finger joints appear to be regulated by BMI, offering a novel hypothesis for the heightened risk of hand OA in obesity.

P 21

Omega-6 Arachidonic acid is increased in Osteoarthritis Bone Marrow Adipose Tissue and negatively impacts osteogenesis.

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Purpose: Osteoarthritis (OA) is a degenerative joint disease marked by subchondral bone remodeling and cartilage degeneration. In human OA, omega-6 lipids have been implicated in exhibiting a pro-inflammatory effect in cartilage and synovial fluid. However, the lipid species secreted by Bone Marrow Adipose Tissue (BMAT) and their role in OA remain unclear. This study aims to profile BMAT lipids in OA subchondral bone and assess their impact on osteogenesis.

Methods: Lipidomic analysis of eicosanoid species was performed on the secreted media of non-sclerotic and sclerotic OA knee bone explants (n = 7). In vitro stimulation for 7 days using osteoblasts isolated from OA samples (n = 5) with omega-6 arachidonic acid (AA) or omega-3 eicosapentaenoic acid (EPA), or co-culture with primary mature bone marrow adipocytes (n = 4). Viability (TP53), bone marker (ALPL) and inflammation (IL-6, IL-8) levels were assessed through qPCR. Osteogenesis, lipid uptake and viability were validated with ALP, Nile Red staining and LDH assay.

Results: Lipidomics identified increased AA (+71%; p = 0.08) versus decreased EPA (-31,9%; p = 0.04) in sclerotic samples. Osteoblasts showed lipid uptake in the presence of AA and EPA and with adipocyte co-culture. No lipotoxicity was observed in any of the conditions. Opposite effects were observed for AA and EPA on osteogenic and inflammatory genes. With AA, ALPL gene expression decreased significantly (0.5 fold; p = 0.0226), accompanied by an increase in IL6 (2 fold; p = 0.0011) and IL8 (8 fold; p = 0.0048). In the presence of EPA, IL6 was reduced (0.5 fold; p = 0.0449). Finally, we also found a strongly decreased ALP staining in the co-culture experiments.

Conclusion: BMAT-secreted lipids are taken up by osteoblasts and exert species-dependent effects on osteogenesis and inflammation. Taken together, these data suggest that lipids secreted by BMAT, specifically omega-6 arachidonic acid, may play a role in aberrant bone formation in OA.

P 22

HOXD10, HOXD11 and HOXD13 as site specific regulators of synovial fibroblasts: Implications for joint-specific pathogenesis

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Background: Rheumatoid arthritis (RA) follows a characteristic joint involvement pattern. Limb and joint embryonic development may influence the susceptibility of certain joints to arthritis. Previously, we showed HOX genes are differentially expressed between joint locations, allowing the assignment of synovial fibroblasts (SFs) to their correct joint location.

Objectives: To decipher the function of HOXD10, HOXD11, and HOXD13 in SFs.

Methods: Synovial tissues (ST) were isolated from RA and osteoarthritis (OA) patients. Cultured SFs from RA finger (n = 2), shoulder (n = 2), and knee (n = 2) underwent ATAC-seq. HOXDs (10, 11, 13) expression was assessed in ST and SFs from hand joints compared to elbow, shoulder, and knee at mRNA and protein levels. Expression was measured in MCP, PIP joints of digits II-V, wrists, and the CMC joint of digit I. SFs were transfected with GapmeR to silence HOXDs or with control GapmeR. Cell adhesion and proliferation of HOXD-silenced SFs were analyzed using xCELLigence RTCA. SFs from hand and knee were stimulated with bFGF for 24 and 48 hours. EdU incorporation was detected with Click-iT Plus EdU, and images were captured using a Cellinsight CX7 platform.

Results: Elevated expression of these genes in cultured SFs from hand joints compared to other sites was confirmed at both mRNA and protein levels. This pattern was also seen in ST, with the most significant difference between hand and knee joints. Expression was prominent in MCP and PIP joints of digits II-V and wrists but not in CMC I. Chromatin regions in HOXD10 and HOXD13 genes were accessible in finger SFs. HOXD10 displayed an open chromatin state in knee SFs, suggesting inducible expression. TNF-stimulated SFs from shoulder and knee showed increased chromatin accessibility in these genes, especially HOXD10. HOXD13-silenced cells showed no changes in attachment but significantly decreased proliferation and reduced Edu incorporation compared to control SFs. MCP/PIP II-V SFs had more Edu-positive cells compared to CMC I, shoulder, or knee joints. Stimulation with FGF for 48 hours significantly increased MCP SF proliferation compared to knee SFs.

Conclusion: In SFs, the 5′-located HOX genes HOXD10, HOXD11, and HOXD13 are highly expressed in posterior-distal limb parts. TNF stimulation may alter chromatin accessibility in these genes. Higher HOXD13 expression in distal joints may enhance hand SF proliferation, contributing to RA development in specific joints.

P 23

Longitudinal Monitoring of Joint Swelling in Rheumatoid Arthritis Through Dorsal Finger Fold Recognition on Hand Photos: Challenges in a Real-World Setting

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Background: Remote Patient Monitoring (RPM) of Rheumatoid Arthritis (RA) patients typically involves the collection of Patient Reported Outcomes via apps, wearables and sometimes blood self-sampling. An objective measure of joint swelling via the previously reported automated detection of dorsal finger fold patterns from hand photographs, could enhance RPM accuracy in RA.

Objectives: To test the quality of automated detection of finger joint swelling based on finger fold recognition in sequentially taken hand photos of RA patients during regular rheumatology consultations.

Methods: We utilized a Convolutional Neural Network (CNN) trained on photos of 1,783 Proximal Interphalangeal (PIP) joints from RA patients to quantify finger folds and PIP joint diameters at the pixel level. The Finger Fold Index (FFI) was calculated as the ratio of joint diameter to the mean pixel length of detected finger folds. We analyzed 74 smartphone images of 17 RA patients taken in ≥2 regular consultations at a Swiss Academic Center. Active disease in at least one visit with congruent hand imaging as well as recorded swollen and tender joint counts and DAS28-CRP scores were required. We describe misclassifications based on algorithm steps.

Results: The algorithm initially captured 222 PIP joints. Of those, 32% were optimally processed in terms of cropping, diameter, and finger fold recognition. The main reason for misclassifications were poor image quality leading to suboptimal cropping (9%), diameter recognition (18%), and incorrect finger fold identification (5%). In 15% of joints, the algorithm failed to provide results. For FFI correlation with joint swelling and DAS28-CRP evolution, seven patients (mean age 53) where monitored across 18 visits, yielding 31 hand images. In 71% of patients (5 out of 7), the FFI correlated with disease progression as indicated by DAS28-CRP changes or swollen joint count. In repeated analyses of healthy hand images, we found that light conditions and positioning of the camera was key for optimal image processing.

Conclusion: Longitudinal finger fold recognition (FFI) in a real-world setting shows consistent results with DAS28-CRP and or swelling and pain on a single joint level. Insufficient image quality was an important cause for misinterpretation in this real-world setting. Improved quality via the use of flash, photo boxes and further training of the algorithm may lead to a higher accuracy for the detection of disease flares.

P 24

Choosing the right score: the critical role of disease activity metrics in RA treatment outcomes with JAK and IL-6 inhibitors – an international multi-register study from the JAK-pot collaboration

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Background: Disease activity scores are pivotal for both treatment guidance and research outcomes in rheumatoid arthritis (RA). However, variations among scores can arise from different components and cut-offs. IL-6 inhibitors (IL-6i) notably reduce acute phase reactants crucial for DAS28, unlike other scores. The effect of JAK inhibitors (JAKi), which also target IL-6, on these scores is less understood.

Objectives: To assess JAKi's impact relative to IL-6i and TNF inhibitors (TNFi) on CDAI, SDAI, DAS28-ESR4v, and DAS28-CRP4v.

Methods: Patients from 12 RA registers in Europe and Québec using JAKi, TNFi, or IL-6i, with available data on four scores, were analysed. Groups were matched by propensity scores on baseline characteristics. Transitions between 4 disease activity states (remission, low, moderate, high disease activity) were investigated using multi-state models (Markov) to derive the (1) mean time spent in a state, (2) hazard ratio of time to transition for IL-6i and JAKi compared to TNFi, and (3) probability of transitioning to a state within 1 year.

Results: In a cohort of 7429 patients:

Time spent in remission was the longest with DAS28-CRP, followed by DAS28-ESR, CDAI and SDAI. CDAI showed the least variation in time spent in each state across treatments, while DAS28-ESR showed the most. IL-6i significantly increased the time spent in remission and, conversely, decreased the time spent in high disease activity, irrespective of the score but more strongly when using both DAS28 scores. This effect was not seen with JAKi.

Compared with TNFi, hazard of transition to a lower score (improving) were significantly more frequent with IL-6i, especially with DAS28-ESR, and, to a lesser extent, with JAKi.

The probability of reaching remission within 1 year was higher with DAS28-ESR and DAS28-CRP (≈50%) compared to CDAI and SDAI (≈25%), regardless of the treatment. IL-6i consistently demonstrating a higher probability of achieving remission at 1 year compared to TNFi and JAKi when using SDAI, DAS28-ESR, and DAS28-CRP.

Conclusion: JAKi had more effects on disease activity states, including acute phase reactants, than TNFi and abatacept, although these effects were only slight and less significant than those of IL-6i. CDAI emerges as the most stable measure across treatments, underlining the need for careful selection of score that do not rely on acute phase reactants in clinical and research settings, particularly when using treatments like IL-6i.

P 25

Infections in patients with rheumatoid arthritis treated with JAK-inhibitors compared to bDMARDs: findings from an international collaboration of registers (the "JAK-pot" study)

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Background: The safety of Janus kinase inhibitors (JAKi), especially regarding infection risks, is a concern for rheumatoid arthritis (RA) patients. Initial pivotal and safety trials reported higher incidences of opportunistic infections and herpes zoster (HZ). However, real-world data on the incidence and severity of these infections remains actively studied.

Objectives: To assess the incidence of infections (any and serious) and HZ in RA patients treated with JAKi, compared to other biologic agents in a large multi-country real-world population.

Methods: We studied patients from 14 RA registers across Europe and Québec, starting on JAKi, TNF-inhibitors (TNFi), or bDMARDs with other modes of action (OMA). Outcomes included all infections, serious infections, all infections excluding HZ, and HZ. Infections were linked to treatments within 3 months of cessation (1 year after initiation for rituximab) or until follow-up loss, death, or study end. Incidence rates (IR) per 100 patient-years (PY) with 95% confidence intervals (CI) were computed. Poisson regressions with propensity score weighting were performed within each register and combined using random-effect meta-analysis to obtain adjusted incidence rate ratios (aIRR) with 95% CI.

Results: Among 54,905 treatment initiations in 36,838 patients with an average follow-up of 2.8 years, there were 7,070 incident infections, including 1,379 serious infections and 352 HZ cases. The crude incidence of any infection was lower for TNFi (7.0/100PY) than for JAKi (9.0/10PY) and OMA (10.6/100PY). Adjusted regression showed no significant difference in the incidence of any infections (aIRR = 1.13; 95% CI [0.91; 1.40]) or serious infections (aIRR = 0.99; 95% CI [0.71; 1.39]) between JAKi and TNFi. However, the incidence of any infection was higher for OMA vs. TNFi (aIRR = 1.20; 95% CI [1.09; 1.32]). The incidence of HZ was significantly higher for JAKi (aIRR = 2.27; 95% CI [1.71; 3.02]) but not for OMA (aIRR = 1.07; 95% CI [0.74; 1.55]) compared to TNFi.

Conclusion: In a real-world study of 14 RA registers with all available JAKi, we found no significantly higher risk of infections, serious or otherwise, in RA patients treated with JAKi compared to TNFi. However, there was a higher risk of any infections with OMA. The incidence of HZ was significantly higher in patients on JAKi compared to TNFi. Planned subgroup analyses will focus on at-risk populations, specific medications, and infection types to guide treatment choices.

P 26

Automated Detection and Quantification of Hand Joint Swelling in Rheumatoid Arthritis Using Computer Vision and Deep Neural Networks: A Potential Biomarker for Disease Activity Monitoring

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Background/Purpose: We have previously shown that automated detection and processing of dorsal finger fold patterns from hand photographs can be used as a digital biomarker for joint swelling in rheumatoid arthritis [1].

In this study, we tested different computer vision and deep learning methods for the automated quantification of dorsal finger folds and diameter of proximal interphalangeal finger joints (PIP) in patients with rheumatoid arthritis. Additionally, the selected model aimed to evaluate the difference in PIP finger joint swelling between healthy individuals and rheumatoid arthritis patients.

Methods: We evaluated the detection and measurement of PIP joint diameter and dorsal finger fold length on hand photographs in 1783 joints of patients with rheumatoid arthritis by canny edge or ridge detection computer vision models or a newly trained convolutional neural network, respectively. The models have been trained to calculate the finger fold index (FFI, potential biomarker for joint swelling), defined as the ratio between pixel length of joint diameter and mean recognized finger folds. In an independent healthy control dataset, the FFI has been calculated to be compared with rheumatoid arthritis PIP joints.

Results: Canny edge and ridge detection were suitable models to detect dorsal finger fold patterns. The prediction of joint diameter and finger fold pixel length was best achieved in a newly trained deep neural network model, where the FFI was predictable in 93% of the images. The accuracy of correct detection of joint diameter measurement was 91%. In 1783 PIP joints of patients with rheumatoid arthritis, the mean FFI was significantly higher than in 168 healthy controls PIP joints (3.42 ± SD 1.04 and 2.15 ± SD 0.68, respectively, p-value < 0.05).

Conclusion: Finger fold index calculated by a deep neural network model seems a reliable tool for the metrical analysis and thus gradeless detection of swelling in patients with rheumatoid arthritis. Standard deviation for FFI in patients with rheumatoid arthritis was higher than in healthy patients. Therefore, further investigation by stratifying patients into different disease activity levels as well as the correlation of FFI with longitudinal changes of clinical scores on a joint-level and general disease activity is ongoing.

Reference

1. doi: 10.1159/000525061.

P 27

Population pharmacokinetic modelling of oral upadacitinib: a real-world prospective observational study

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Introduction: Upadacitinib is a small molecule targeting selectively JAK1 protein and used orally for the treatment of inflammatory bowel diseases, rheumatological, and dermatological disorders. Dose-response relationship and exposition-dependent tolerability issues have been reported. We hypothesize that efficacy and safety, including adverse events of special interest, could be improved by optimizing upadacitinib exposure based on plasma concentrations coupled with a population pharmacokinetic (popPK) model. As part of our nationwide prospective observational study, we aim to build a popPK model to describe the typical PK profiles and characterize the interindividual variability (IIV), while identifying patient-related factors influencing upadacitinib exposition.

Methods: Adult patients (>18-year-old) receiving upadacitinib for disease control were enrolled in our study either for detailed PK investigation (serial blood samples over 8h) or for sparse sampling collected at unselected times after the last drug intake during routine follow-up. Covariates such as age, sex, bodyweight (BW), body mass index (BMI) were recorded. PopPK modelling and simulation were performed with NONMEM®.

Results: A total of 90 plasma concentrations of upadacitinib were measured in 31 patients with axial spondylarthritis (n = 6), psoriatic arthritis (n = 5), rheumatoid arthritis (n = 2), Crohn's disease (n = 7), ulcerative colitis (n = 4), atopic dermatitis (n = 2), and other autoimmune disorders (n = 5). The detailed PK investigation and the sparse sampling study included 7 and 24 patients. Subjects were predominantly female (69%), with a median age of 48 years (range: 19-87 years) and a median BMI of 26.6 Kg/m2 (range: 19.6-43.1 Kg/m2). Dosages of upadacitinib ranged from 15 mg to 45 mg per day. A one-compartment model with change-point absorption and linear elimination best described upadacitinib data. Moderate IIV was observed on clearance (38.5%), that significantly decreased of 35% in patients of 50 kg compared to 70 kg individuals.

Conclusion: Our findings reveal an important role of BW on upadacitinib PK in the patient population. Given the narrow therapeutic margin and high PK variability, the implementation of therapeutic drug monitoring for upadacitinib and modelisation frameworks could address dose-dependent efficacy and safety issues. Further observations are needed to determine disease-specific therapeutic intervals to leverage upadacitinib effectiveness.

P 28

Impact of early versus late DMARD initiation on permanent loss of gainful employment in patients with rheumatoid arthritis – a retrospective analysis in a Swiss patient cohort

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Background: Rheumatoid Arthritis (RA) is a prevalent inflammatory disease causing joint damage, pain and disability, significantly impacting patients' ability to maintain gainful employment. Addressing work ability in RA patients is essential for improving their quality of life and reducing RA associated societal and economic burdens. While new treatments, including disease-modifying antirheumatic drugs (DMARDs), have improved outcomes, the impact of early versus late DMARD initiation on employment status remains unclear.

Objective: The primary study objective was to assess whether early DMARD initiation (within one 1 year of symptom onset) reduces the risk of permanent loss of gainful employment (LOGE) due to RA compared to late initiation (one 1 to five 5 years after symptom onset) in Swiss RA patients. The secondary objective was to assess the overall risk of LOGE in this population.

Methods: A retrospective analysis was conducted using data from the SCQM registry. RA patients aged 18-63 with gainful employment at symptom onset and known seropositivity status were included. The outcome for both objectives was time from symptom onset to permanent loss of employment due to RA. A cause-specific proportional hazards model was used, adjusting for year of symptom onset, sex, age at symptom onset, seropositivity and educational level. The data were interval censored and left truncated.

Results: The study included 1489 patients, with 935 in the early DMARD group and 554 in the late DMARD group. We observed no evidence for a difference in the hazard of permanent employment loss between early and late DMARD initiation groups (HR = 0.82, 95% CI 0.59–1.15). A later symptom onset (with respect to calendar year) and higher levels of education were associated with lower hazards of LOGE, whereas increasing age at symptom onset was associated with a higher hazard. We estimated that almost 1 in 5 typical RA patients lost their permanent employment within 10 years, regardless of DMARD initiation timing.

Conclusion: We found no evidence of early DMARD initiation reducing the risk of permanent loss of gainful employment compared to late initiation. Factors such as educational level and age at symptom onset seem to play a crucial role in employment outcomes. Further prospective studies and quality data are needed to confirm these findings, to define accurate strategies to improve work ability as they are linked to better health outcomes and overall quality of life for these patients.

P 29

Management of SAPHO syndrome in daily practice: Cross-sectional study on 44 patients

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Introduction: SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis) is a rare entity which designates the association of a heterogeneous set of cutaneous and osteoarticular manifestations having as a common denominator an aseptic inflammatory process.The frequency of this syndrome in the

population is difficult to assess due to the lack of a precise inventory of proven cases in the literature. It must consider all the clinical and radiological elements, especially since the appearance of dermatological signs is not necessarily concomitant with that of osteoarticular symptoms. Managing this syndrome is not always easy because there are no clear treatment recommendations. Therapeutic strategies for this syndrome are based on the results of uncontrolled trials carried out on groups.

Objective: This study aims to assess the socio-demographic characteristics, the clinical and paraclinical profile as well as the therapeutic management of our patients seen in consultation.

Patients and Methods: This is a cross-sectional study involving patients followed for SAPHO syndrome seen in our rheumatology department over a period ranging from 1998 to 2022. Only patients with an established diagnosis of SAPHO were selected.

Results: We collected 44 patients. The mean age was 38 years, with a female predominance (70%). The mean weight was 73 kg. comorbidities were present in 17 cases (38,6%). Regarding the location of the SAPHO, 22% was the sternoclavicular joint, 13% was the sternum, 11% was the manubrio-sternal joint, 9% the clavicle. Moreover, 25% have sacroillitis, 15% have spine involvement, 2% the long bones. Regarding imaging, the diagnosis of SAPHO was made in 12 patients (27,3%) by conventional X-rays, 27 (61,3%) patients had a positive MRI, 14 (31,8%) a positive CT scan, and we confirmed the diagnosis of SAPHO by bone scintigraphy in 18 patients (40,9%). For therapeutic aspects, 20 patients (45,4%) out of the 44 cases were on pamidronate from the diagnostic with a remission in 80%. 44% patients received biological agents, in this case an anti-TNF alpha (infliximab) or anti-IL17A with 100% remission.

Conclusion: Management of SAPHO syndrome remains difficult in daily practice due to the lack of clear recommendations for its assessment. Our study was able to identify a larger number of patients and was able to demonstrate the important role of anti-TNF and anti-IL17 in the therapeutic management of this pathology

P 29.1

The contribution of ultrasound in enthesitis of psoriatic arthritis

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Introduction: Ultrasound plays an important role in the diagnosis at an early stage of the various enthesitis lesions in psoriatic arthritis (PsA). The objective of this work was to evaluate its contribution to this achievement.

Materials and methods: This is a retrospective single-center descriptive study carried out in the rheumatology department at the university hospital over 7 years. Patients with psoriatic arthritis in its peripheral form were included. Patients in whom the diagnosis of rheumatoid arthritis (RA) could not be eliminated due to the difficulty of the differential diagnosis between these two pathologies were excluded.

Results: Sixty patients were included. The average age was 48.18 with a clear female predominance (M/F sex ratio: 0.93). For comorbidities, 18.2% of patients were diabetic, 13.6% were hypertensive, 6.8% had heart disease, 45% were monitored for nephropathy. 81.8% of patients had known skin psoriasis, 11.4% had familial psoriasis and 6.8% were free of skin involvement. The average duration of disease progression was 9.89 years. Enthesis affected 28 patients, it was mainly inflammatory heel pain in 33% of cases, 35% had inflammatory buttock pain, a minority had pain in the epicondylar region and in the plantar aponeurosis. Ultrasound of the entheses was done for diagnostic purposes in 55% of patients. The ultrasound study showed that 23% of patients had no entheseal damage, 5% had periosteal apposition, 23% had epicondylar enthesitis, 26% Achilles enthesitis, 14% plantar aponeurosis, 8% at the level of enthesis of the quadriceps tendon, 3% an enthesophyte of the flexors, and 3% an enthesitis at the level of the enthesis of the patellar tendon

Conclusion: Our study is consistent with the results of the literature, enthesis damage was detected on ultrasound in our patients. Ultrasound of entheses seems to be useful in the differential diagnosis between RPso and RA. The identification of these extra-synovial lesions points towards the diagnosis of PsA.

P 30

Persisting gender disparities in rheumatology research: an analysis of authorship trends in randomised controlled trials

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Objectives: This study aims to examine the evolution and influencing factors of women's authorship in randomised controlled trials (RCTs) publications in rheumatology.

Methods: This study included all rheumatology RCTs published since 2009 using MEDLINE Cochrane Highly Sensitive Search Strategy. Gender was determined using forenames and countries of affiliation via the gender API service. The primary outcome was the gender of authors, with covariates including the RCT's continent, international collaboration status, industrial funding, intervention type, sample size, journal adherence to ICMJE recommendations, impact factor, publication year, author's non-academic affiliation, and author position. Statistical analysis involved generalised estimating equations, assessing the percentage of women in RCT publications and the impact of covariates. Two models were used: one examining factor influencing a woman being an author, and another including the gender of the last author as an additional covariate.

Results: Analysis of 1,109 RCTs authored by 11,103 persons revealed that women accounted for 39.5% (95%CI 38.0-40.9%) of authorship. Significant geographical disparities were observed, with African-based RCTs showing a higher likelihood of female authorship compared to North America, while Asian and European-based RCTs had lower odds. The odds ratio (OR) of the last author (0.72 [0.61-0.86]; -7.3pp) and pre-last author (0.70 [0.60-0.83]; -8.0pp) being a woman was lower but not first of second. There were fewer women authors in industry-funded RCTs (OR 0.65 [0.56-0.75]; -9.8pp). There were no difference looking at international status or RCT sample size. Non-academic affiliation increased the chance of having a woman author. There were no changes in the proportion of women authors by year of publication. Having a woman last-author increased the odds of having a woman first author (1.54 [1.10-2.17]; +10.4pp).

Conclusion: The overall presence of women authors was 39.5%, with significant variations observed based on geographic region, authorship position, affiliation, and funding source. Positions like last or pre-last author were less likely to be held by women, highlighting a gender gap in senior roles. RCTs with a female last author were more likely to have a female first author, suggesting a potential role-model effect. The

stagnant year-over-year representation of women in RCTs underscores the urgent need for more effective strategies to bridge the gender gap.

P 31

A guide for establishing meaningful collaborations between patient research partners and researchers in rheumatology

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Background: Patient research partners (PRPs) are people living with a relevant disease who actively contribute to research. Their contribution is beneficial for any research project (1). Although the inclusion of PRPs in rheumatology research is increasingly recommended, its practical implementation, particularly in translational research, remains limited (2). Enhancing PRP engagement requires a clear understanding of the necessary steps.

Objective: This study aims to show steps to achieve successful collaboration between PRPs and researchers and its benefits and challenges in clinical and translational research in rheumatology.

Methods: We established a PRP network by following five main steps: setting up infrastructure, recruitment, training, PRP involvement at an early stage, and ongoing support. We adhered to overall principles of openness, feedback, and regular evaluations to create a respectful and collaborative environment. The initiative was qualitatively assessed via an online questionnaire developed by each six researchers and PRPs.

Results: Communicating our initiative at laboratory open days and to patient associations has enabled to create a network of over 60 PRPs. A match-making tool was introduced to allocate interested PRPs with a project request. This led to PRP involvement in 14 projects, including 9 in translational research. Two PRP-coordinators provided support including glossaries and educational courses (45 PRPs and over 30 researchers were trained). 52 PRPs and 24 researchers completed the questionnaire. PRPs and researchers found the training useful, enhancing their knowledge and confidence in research collaboration. PRPs identified benefits of the initiative such as better research comprehension, improved coping with illness, valuable engagement with others, and empowerment. Reported barriers were short timelines, inequalities among PRPs, and insufficient information. Researchers highlighted initiative's benefits like easy access to facilitated PRPs, gaining patient perspectives, and adopting a patient-centered approach. They faced uncertainty in PRP involvement in laboratory based projects and lack of diversity in PRPs.

Conclusions: Our initiative outlines five essential steps for establishing PRP collaboration in rheumatology research, including translational research. This approach benefited both PRPs and researchers and might serve as a guide for other centres.

1. de Wit MP et al. Ann Rheum Dis.(2011).
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P 32

Prospective Registration of Trials in Rheumatology: Where we are, why, and how we could get better.

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Importance: Transparent trial conduct requires prospective registration of a randomized controlled trial before the enrolment of the first participant. Registration aims to minimize potential biases through unjustified or hidden modification of trial design during the study. The uptake of this good practice varies between fields of medicine.

Objectives: We aimed to (1) estimate the proportion of randomized controlled trials in rheumatology that are prospectively registered and determine the time trends and the factors associated with prospective registration; (2) evaluate the reasons for non-adherence with prospective registration and explore potential mechanisms aimed at enhancing adherence with prospective registration.

Design: Reports of trials in rheumatology published between January 2009 and December 2022 were retrieved using MEDLINE-PubMed. We retrieved trial registration numbers using metadata and reviewing full texts. We conducted a multivariable logistic regression to identify factors associated with prospective trial registration. For RCT that were not prospectively registered, using an online survey sent to the authors we inquired about possible reasons for nonadherence with prospective registration and explored their opinion about potential solutions.

Results: We identified 1093 primary reports of randomized controlled trials, with 453 (41.4%) that were not prospectively registered, with 130 (11.9%) not registered and 323 (29.5%) were retrospectively registered. The proportion of trials prospectively recorded increased over time at a rate of 3% per year ($p < 0.001$), with only 13.3%(2/15) trials prospectively registered in 2009 to 73.2% (112/153) trials in 2022. In the adjusted model, the factors positively associated with prospective registration were a larger sample size, recruitment conducted across countries, evaluation of pharmacologic interventions, and being published in a journal with higher impact factor. Investigators reported mainly lack of knowledge, or organizational problems as the main reasons for retrospective registration. Authors also suggested that linking the obtention of ethic approval to trial registration is the best option to ensure prospective registration.

Conclusions and relevance: Despite significant improvement, adherence with prospective registration remains unsatisfactory in rheumatology. Different strategies targeting both journal editors and healthcare professionals and researchers may improve trial registration.

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Disease Characteristics of Fibromyalgia Patients with a Concomitant Immune-Mediated Rheumatic Disease

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Background: The coexistence of fibromyalgia (FM) with immune-mediated rheumatic diseases (IMRD) is frequent and complicates their diagnosis and treatment. Often referred as secondary FM, it is unclear if fibromyalgia in IMRD patients differs from primary FM.

Aim: The study aims to compare the characteristics of FM patients with and without IMRD and to assess the equivalence of different diagnostic criteria in a context of concomitant FM.

Methods: A comprehensive dataset of clinical, psycho-social and sleep variables was collected in 341 patients with chronic musculoskeletal pain syndromes undergoing a rheumatology-led two-week multimodal inpatient program at the University Hospital of Lausanne from 2018 to 2024. Participants were included either with fulfilled ACR 2010 criteria or Fibromyalgia Rapid Screening Tool (FiRST). IMRD diagnosis was performed by the treating rheumatologists, before the multimodal treatment.

Results: We identified 153 patients with documented fulfilled ACR 2010 criteria, of those 32 also had a history of an IMRD. The FiRST criteria were fulfilled in 149 patients, of whom 34 also had IMRD. The majority of IMRD were HLA-B27 negative spondylarthritis (SpA) (53%), Sjögrens syndrome (16%), HLA-B27 positive SpA (9%), psoriasis arthritis (9%), seronegative- (9%) and seropositive rheumatoid arthritis (3%). No significant differences in patient characteristics were found between those with and without IMRD, except for the presence of enthesopathies, childhood pain and therapy with Prednisone, DMARDs or biologics. Nociplastic pain was most prevalent in both groups, without a difference in inflammatory pain. Patients with concurrent IMRD had slightly lower FiRST scores and responded better to the multimodal pain program in terms of FABQ work, BPI interference and Pain Catastrophizing Scale, compared to primary FM patients. FiRST and ACR2010 criteria were equally valid to define FM.

Conclusion: Similar clinical profiles are observed between FM patients with or without concomitant IMRD, suggesting a common pathomechanism of FM.

P 34

Exploring vaccination behaviour in patients with rheumatic diseases: findings from a registry-based study (Swiss Clinical Quality Management).

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Background: In patients with inflammatory rheumatic diseases (IRD), the heightened infection risks due to both the diseases themselves and the immunosuppressive nature of their treatments underscores the critical need for effective vaccination strategies in this vulnerable population.

Objectives: To explore and evaluate the belief, attitude, and behaviour of patients with rheumatic inflammatory diseases around vaccination, utilizing data from a national register in Switzerland.

Methods: In this cross-sectional survey of patients with IDR from the Swiss Clinical Quality Management (SCQM), a questionnaire to assess attitude and behaviour around vaccination was developed. The main outcome was vaccination uptake evaluated through three parameters: updated vaccination status, influenza vaccination coverage and pneumococcal vaccination coverage. The main exposures evaluated were patients' perceived importance of vaccination and their beliefs regarding vaccination safety. Patients registered in SCQM and who responded to these two specific questions were included in the analyses. Descriptive analyses were the mean and standard deviation for continuous variables and frequency for categorical variables. Missing data were imputed by multiple imputation and the associations were estimated using logistic regression.

Results: Of 2673 patients analysed, 60% were women and 77% <65 years old. While 52% believed both in the importance and safety of vaccine, 2% believed both that vaccination is not safe and that is not important to follow the recommendations. Most patients (64%) didn't change their vaccination beliefs after the COVID-19 pandemic. Among respondents, 47% had checked their vaccination status in the last 24 months, 51% had coverage against influenza and 33% against pneumococcal pneumonia. Discussions with the rheumatologist about vaccination or before initiating treatment and increased willingness to be vaccinated since the COVID-19 pandemic were significantly associated with vaccination.

Conclusions: Rates of self-reported vaccination were relatively low in this vulnerable population. Discussion with the rheumatologist about vaccination and patient's beliefs were associated with vaccination rates. Strategies specifically targeting these factors can play a pivotal role in improving vaccination rates among patients with IRD.

P 35

SARS-CoV-2 seroprevalence and risk of asymptomatic infection in patients with inflammatory rheumatic diseases compared to the general population prior to COVID-19 vaccination

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Objective: Patients with immune-mediated rheumatic musculoskeletal diseases (RMDs) are at increased risk of severe COVID-19, due to their condition and treatment with immunosuppressive drugs. The rate of asymptomatic SARS-CoV-2 infection is unknown in this population. We aimed to compare the seroprevalence and risk of developing an asymptomatic SARs-CoV-2 infection between patients with RMDs and the general population prior to COVID-19 vaccination.

Methods: Adult patients with inflammatory RMD from the Swiss Clinical Quality Management (SCQM) cohort were included and asked to report on symptoms related to COVID-19 on a monthly basis. Serological samples for anti-SARS-CoV-2 IgG were obtained via self-collection kits. Exact matching was performed between SCQM patients and participants from Corona Immunitas, a Swiss national multicentric seroprevalence study including randomly selected adults from the general population. Participants were matched for the date of serology (year and

month) and the geographic localisation (German-, French-, and Italian-speaking regions of Switzerland). Operationally, we defined asymptomatic SARS-CoV-2 infection as a positive anti-SARS-CoV-2 IgG test without concurrent or prior self-reporting of COVID-19 related-symptoms (anosmia/ageusia, shortness of breath; cough; sore throat; runny nose; fever; headache; myalgia; fatigue; diarrhoea).

Results: 1465 SCQM and 8855 Corona Immunitas participants were included, of which 1436 and 6764, respectively, could be matched. We included individuals sampled between August 2020 and March 2021, prior to COVID-19 vaccination. The SARS-CoV-2 IgG seroprevalence was 78/1436 (5.4%) in RMD patients and 874/6764 (12.9%) in matched control participants. The odds of contracting SARS-CoV-2 was significantly lower in RMD patients (OR 0.53, 95% CI 0.41-0.67). The rate of asymptomatic infections was similar between RMD patients and controls (14/76, (18.4%) versus 125/544 (23%); OR 0.76, 95% CI 0.40-1.36).

Conclusion: Seroprevalence for SARS-CoV-2 was lower in RMD patients compared to the general population, most likely due to special precautions taken by RMD patients during the COVID-19 pandemic. In this study, no evidence was seen for a difference in asymptomatic SARS-COV-2 infections between RMD patients and the general population.

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Which exercise modalities for people with osteoarthritis: An open access website with interactive visualisation and meta-analysis.

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Introduction: Exercise is recommended by guidelines for treating osteoarthritis (OA) in the knee and hip. Identifying which patients benefit most from which specific types of exercise remains unclear. While numerous systematic reviews exist, an up-to-date, open-access database with comprehensive data on study, intervention, and patient characteristics, coupled with interactive tools for analysing outcomes, is lacking. Our goal was to develop a webpage that integrates data pipelines from publications to interactive visualizations. The long-term objective is to automate processes for sustainable database updates with minimal resources. The website includes features for data entry, control, and modification, all secured with authentication (dedicated usernames and passwords) and an audit trail (tracking modifications and deletions). Given the exploratory nature of interactive analyses, we will establish guidelines and moderated sections to ensure accurate interpretations.

Methods: As a first step, we focused on randomized trials examining exercise for individuals with hip osteoarthritis, using an umbrella review approach. Data for the interactive meta-analysis were extracted from meta-analyses and original studies. We developed two search strategies tailored for Medline (Ovid), Embase, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL): one for randomized trials and one for systematic reviews. For this congress, we screened only systematic reviews, with each title/abstract and full-text reviewed independently by two reviewers. We established a database, a web-based data entry form with authentication and an audit trail, filterable and searchable tables, and interactive visualizations for meta-analysis. These visualizations support subgroup analyses based on risk of bias, intervention type or duration, follow-up time-point, intervention contrast, funnel plots, and allow changes in meta-analysis methods (e.g., common/fixed effect, random effects, tau estimation methods). Additionally, we developed adaptive text modules to guide the interpretation of results, considering the exploratory nature of these analyses.

Results: Users can now interactively filter and modify meta-analyses for exercise interventions in individuals with hip osteoarthritis. The website facilitates accurate interpretation by providing structured guidance and tools for comprehensive data analysis. The interactive website can be found at https://www.reuse.rehab/oa/.

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Development and implementation of gout quality criteria in an electronic health record-based gout register: a feasibility study

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Introduction: Gout, the most common inflammatory arthritis, is often undertreated. It is associated with an increased mortality, can lead to permanent loss of function and more frequent hospitalisation. There is a lack of high-quality data on current management quality, particularly outside specialized rheumatology settings. We outline the development of electronic quality criteria from existing guidelines and their application to an electronic health record (EHR)-based gout register for both in- and outpatients.

Methods: We selected all grade A and B recommendations from the 2016 European Alliance of Associations for Rheumatology (EULAR) and 2020 American College of Rheumatology guidelines for gout management, as well as the 2018 EULAR recommendations for gout diagnosis. We then assessed the recommendations for feasibility of implementation in an EHR-based gout register from the Geneva University Hospital, containing 5'138 patients as of 31.12.2022, and show results for two criteria.

Results: The 3 sets of guidelines contained 61 recommendations corresponding to 87 statements associated to a grading of evidence. Of the 55 statements with grade A or B evidence, 10 were excluded because of redundancy with other criteria, and 24 because they were judged not implementable. Of the remaining 21 criteria, 4 were related to acute flare treatment, 3 to flare prophylaxis, 3 to urate-lowering therapy indication (ULT), 10 to recommendations for patient under ULT and 1 to diagnostic. The criteria concerning indication for ULT in patient with recurrent flares (i.e. at least two flares during one year, n = 163) showed a prescription of a ULT in 66.9% of the patients within a year, in patients that visited the hospital again. Among patients with documented tophi (n = 72), 20.8% of patients did not receive a ULT within a year. Regarding diagnostic criteria, 44.9% of patients received a plain radiography of the articulation within 10 days of an acute gout flare proven by a joint aspiration (n = 965).

Discussion: We developed electronic quality criteria for gout management and diagnosis based on existing guidelines. Preliminary results show suboptimal ULT prescriptions and insufficient imaging to assess for urate crystal deposition, which can impact ULT prescription. Applied automatically to an EHR-

based gout register, these criteria will serve as quality indicators, enabling monitoring and assessment of management improvements over time.

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CPP Crystals in Low Back Pain

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Background: Chronic low back pain burdens individuals and societies alike. Disc degeneration, characterized by calcification and calcium phosphate crystal deposition, is a contributing factor in some patients. Among these deposits, calcium pyrophosphate dehydrate (CPP) crystals can episodically trigger inflammatory reactions through the NLRP3 inflammasome, promoting mature IL-1β production and initiating inflammatory cascades. However, aside from rare case reports of acute spinal CPP crystal inflammation, research has mainly focused on their disruptive nature, neglecting their potential for inflammation.

Objective: To explore the role of CPP crystals in chronic low back pain, hypothesizing that their inflammatory potential contributes to pain and disc degeneration beyond mechanical disruption.

Methods: We analyzed 67 discs from 64 from patients undergoing lumbar spinal fusion. Histologic slides were examined with H&E, Masson trichrome, and immunohistochemistry (IHC) for IL-1β. The presence of CPP crystals was compared to patient demographics, pain scales, medical history, and imaging data. Isolated disc cells were cultured and stimulated with two concentrations of CPP crystals (50 µg/mL, 100 µg/mL), and gene expression of catabolic and inflammatory genes was assessed with quantitative real-time PCR (qPCR) after 24 h and 48 h of stimulation.

Results: Dense clusters of CPP crystals were found in about 20% of patients and 21% of discs. Collagen fiber condensation was noted around some clusters. Patients with CPP crystals were significantly older (p = 0.001) and showed trends towards previous herniation (p = 0.082) and surgery (p = 0.067). No IL-1β presence was detected in IHC-stained samples. In vitro, CPP crystals upregulated IL-1β gene expression at 24 hours, and of IL-6, MMP-1, -3, and -13 at 48 hours. ADAMTS5 or CCL2 gene expression did not change.

Conclusion: While CPP crystals are associated with age, herniation, and previous surgeries, and can provoke a phlogistic response in vitro, they likely do not contribute to chronic low back pain via inflammatory pathways in situ. The episodic nature of inflammation or encapsulation might limit their clinical relevance.

P 39

Dominating prevalence Calciumpyrophosphat (CPP) crystals among inflammatory synovial fluid samples in an unbiased analysis at the largest Swiss tertiary center.

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Background: crystal arthritides mainly comprise of gout and calciumpyrophosphat (CPP) Deposition Disease, known as CPPD or pseudogout. The prevalence, medical and socioeconomic impact of gouty arthritis is well recognized and estimated to affect 5% of the population in developed countries. However, while chondrocalcinosis, a non-pathogenic deposition of CPP crystals in cartilage, shows a high and increasing prevalence in persons over 60 years, the prevalence of CPP arthritis in daily practice remains unclear. We herein sought to assess the unbiased prevalences of crystal and crystal arthritides in synovial fluid (SF) samples at the largest hospital in Switzerland.

Methods: We included SF samples, obtained between 2015-2023 at the University hospital Bern (Inselspital), the largest hospital in Switzerland. Samples from all Departments were considered and analyzed, irrespectively of the indication for arthrocentesis and final diagnosis. Crystal analysis was performed by rheumatologists and specifically trained lab personnel. Crystals were assessed based according to negative (MSU) or positive (CPP) birefringence under polarized light as well as positive staining with alizarin red (BCP) under ordinary light microscopy. All results were documented in a semiquantitative manner (little, moderate, massive). In parallel, leucocyte counts including fractions of mononuclear and polynuclear were assessed in most SF samples.

Results: we analyzed 4777 samples from 3239 patients. Crystals were found in 39.2% of all samples, with CPP being detected in 59.3%, while 40.7% were positive for MSU. As for BCP 9.3% of samples stained positive for alizarin red. Cell numbers in SF were available in 2899 samples, among which 1703 (58.7%) were classified as inflammatory (>2000 cells/ul), and 1196 (41.3%) as non-inflammatory (<2000 cells/ul). Among inflammatory samples 38.5% were crystal positive, with CPP predominating with 58.4% versus 41.6% MSU, whereas 7.3% of samples stained positive for BCP crystals. Neither the mean of total leucocyte numbers nor the yields of polynuclear cells were significantly different between MSU and CPP positive samples.

Conclusion: Contrary to the general belief that gout is the most common form of crystal arthritis, our data indicate that CPP arthritis may in fact be the most common cause among multimorbid patients at a tertiary center. To our knowledge this is the largest study assessing the unbiased prevalence of crystals in in SF.

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Performance of a nurse-led outpatient clinic in a real world gout cohort at the largest tertiary center in Switzerland.

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Background: Gout is the most common inflammatory arthritis in Western countries and is sharply increasing in developing countries. Gouty arthritis leads to immobilization, hospitalizations, treatments and work absences, putting a significant on the healthcare systems. Despite the existence of effective urate-acid (UA) lowering drugs, adherence to drugs as well as capacities of management by general and specialized practitioners appear to be suboptimal. Here, we report on the first results eight months after implementation of a nurse-led gout outpatient clinic at the largest university hospital in Switzerland and including patients with complex comorbidities, such as organ transplantation.

Methods: A total of 28 confirmed gout patients were assessed and treated in the outpatient clinic during 66 visits at the largest tertiary center in Switzerland. Follow-up visits were usually scheduled every 2-4 weeks. All patients received a brief assessment by a rheumatologist, In addition, general information regarding non-pharmacological therapy such as dietary and

lifestyle adjustments was provided by a specialized nursing professional. Most of the patients had received little to no comparable information prior to this initial consultation. Modification of urate-acid lowering therapy, addition of anti-inflammatory or other drugs were prescribed by the rheumatologist upon each visit.

Results: 23/28 patients were already on UA-lowering therapy before their first visit. While seven patients were already at their UA-target at their first visit, twenty-one patients were beyond UA target and needed treatment escalation. Among them, 10/21 had a UA target of <360umol/ and 11/21 had a UA target of <300umol/l. UA target levels were reached 6/19 (31.6%) at visit two, an additional 4/11 (36.4%) at visit 3 and 1/5 (20%) at visit 4, respectively. Mean UA levels were reduced from 486.2umol (visit 1) to 398.3umol/l (visit 3).

Conclusion: In line with previous studies in patients with GP profile, our data in tertiary center patients suggests that UA target levels can be achieved within two visits (approximately eight weeks) and within a nurse-led outpatient setting. Loss of adherence was seen in approximately 10% of patients. Expansion and additional follow-up visits of our cohort are necessary to confirm these results and assess effect of UA-lowering therapy on additional life and metabolic parameters.

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Navigating Through Regulatory Frameworks for Digital Therapeutics and Biomarkers

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Background: Digital health solutions are increasingly entering rheumatology with great potential to improve care of patients. These digital health technologies such as digital therapeutics, digital biomarkers or software as a medical device (SaMD) are often subject to regulatory requirements. Regulatory auditing processes are complex but necessary to guarantee quality, efficacy and especially safety of patients. Newer evolvements such as decentralized and digitalized clinical trials, wearables and digital biomarkers require a constant adaption of regulatory frameworks.

Objective: To provide an overview on current regulations and standards for digital therapeutics and digital biomarkers, from technical development to market access.

Methods: We conducted an unstructured literature research on PubMed, industry documents, government guidelines, laws and legislations and international standards to identify the relevant guidelines, policies and standards for software based digital therapeutics and digital biomarkers. Regulations and legislations from the European Union and the United States were included.

Results: The principal regulations governing software as a medical device and digital therapeutics are outlined in Chapter 21 of the Code of Federal Regulations by the US Food and Drug Administration, as well as the European Medical Device Regulation 2017/745. A key quality standard in the development of SaMD is ISO 14971. Regulatory pathways, such as the DiGA , are in the process of development, particularly for digital therapeutics, which fall within the purview of software as a medical device. Qualification of (digital) biomarkers is typically voluntary but can play a significant role in the development and approval of digital therapeutics. Clinical studies are increasingly embracing electronic data management, real-world data, and decentralized clinical trial components. These methodologies are instrumental in generating robust evidence for validating biomarkers, software as a medical device, and digital therapeutics.

Conclusion: Fragmented, lacking and diverse regulations in the area of digital biomarkers and digital therapeutics highlight the urge to harmonize and foster regulatory frameworks on an international level. Future research is needed to analyze regulatory frameworks in other countries and regions as well as the importance of capturing new developments in regulatory science to facilitate the growth of digital health solutions.

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Impact of Patient Profiles and Onboarding Strategies on Engagement in a Chronic Pain Management Mobile App

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Background: Mobile health apps are effective in managing chronic pain syndromes like fibromyalgia, which is increasingly prevalent, especially in post-COVID-19 patients. We developed an app for post-viral chronic pain management, focusing on patient engagement. Understanding the relationship between patient interaction with the app, their clinical and demographic characteristics, and onboarding strategies is essential for refining these tools and enhancing personalized digital health strategies.

Objectives: To explore the correlation between patient engagement in a mobile health app for chronic pain management, their clinical and demographic profiles, and the effectiveness of onboarding strategies.

Methods: A test version of the app was released for iOS and Android, with participants recruited from a multimodal care program for chronic pain. Patients underwent various assessments, including for fibromyalgia, alexithymia, and pain disability. Onboarding was done either remotely (via email) or with nurse assistance. Over four weeks, we collected usability metrics and patient-reported outcomes through the app, with weekly SMS reminders. A System Usability Scale (SUS) questionnaire was administered at the study's end.

Results: Among the first 22 users (15 assisted onboarding, 7 remote), engagement levels varied. Patients ranged from 26 to 63 years, 86% female, 14% male, with an average BMI of 27.83, a Widespread Pain Index of 10.33, and a Symptom Severity Score of 8.67. Most were diagnosed with depression. Engagement averaged 10.13 activations for assisted onboarding versus 8.0 for remote onboarding. Reminders were effective, but 73% stopped using the app after reminders ceased. Three patients discontinued due to a broken smartphone or health decline. Some continued app usage without engaging in the satisfaction survey.

Conclusion: Initial results underscore the importance of a multidisciplinary approach to understanding mobile health app engagement in chronic pain patients. Engagement levels are influenced by onboarding methods, clinical, and demographic profiles. Assisted onboarding promotes higher engagement than remote onboarding. Reminders are effective, but many users discontinue app use after reminders stop. The high prevalence of depression suggests a need for tailored strategies for this group. Further data collection is essential to refine personalized digital health interventions for chronic pain management.

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The mySCQM patient app: insights from eight years of use for self-observation in the SCQM cohorts.

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Background: The mySCQM patient app has been available to patients of the SCQM cohorts since 2016, during which a plethora of patient-reported outcomes have been collected on a weekly or monthly basis. In an international survey on mobile health apps for disease self-management conducted by EULAR in 2023, the highest response rate (31%) came from patients in Switzerland. In this study our aim is to gain insights into the mySCQM user base, the use trends, and their evolution, as a basis for a future study on the effectiveness of self-observation on disease activity and quality of life.

Methods: We retrospectively analyzed the data that were prospectively collected via the mySCQM app. We examined the retention of mySCQM app use, by calculating the Kaplan-Meier estimator of the survival function, where the event of interest (mySCQM discontinuation) was defined as the first time since signing up for app use that a six-month gap with no entry was observed.

Results: Overall, since its launch in 2016 until the end of 2023, 4110 patients (38% axSpA, 35% RA,19% PsA, 7% UA, 1% GCA/PMR) have used mySCQM, entering the app a total of 102000 times. As a result of two major prospective studies related to COVID-19, with remote participation and questionnaires implemented via mySCQM, we observed a 3-fold increase in the number of regular app users, which is currently stable at ~ 2100 per quarter. The median period of mySCQM retention was 2.5 years and 30% of mySCQM users were still using the app after six years, indicating that sustained self-observation is valuable for these patients.

Conclusions: Retention of mySCQM app use is high. There is a positive feedback loop between prospective studies and mySCQM use, with the former leading to an increase in interest and number of patients signing up for the app, and the latter providing a high and sustained user base for direct recruitment into future decentralized studies. Further research will provide insight into the effectiveness of self-observation mySCQM and guide its future development as tool for disease self-management.

ABSTRACTS HPR

HPR 1

Development of nurse-led consultations, supporting patients to self-manage rheumatic diseases and discover personalized strategies for alleviating symptoms

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Rheumatic diseases often present as complex clinical pictures with heterogeneous symptoms and are chronic. In addition to economic aspects, the impacts of these diseases on those affected and their social environment can be significant. Affected persons want to maintain a high quality of life despite their illness and to cope with the symptoms it brings in daily life. To do so, they need sufficient disease knowledge and self-management strategies. Good knowledge about their disease is key for successful long-term treatment of these patients. This is where nurse-led consultations can come in.

In the project described, person-centred consultations and education by an Advanced Practice Nurse (APN) for patients with rheumatic complaints and their relatives is being developed to complement medical consultations. Goals of these nurse-led consultations are to encourage self-management, empower individuals to address their condition independently, and discover personalized strategies for alleviating symptoms.

The development of the nurse-led consultations, as well of the APN role, are based on the PEPPA framework model and fundamental principles of APN as outlined by Hamric. Alongside a literature review, surveys and workshops were conducted with stakeholders, including medical, nursing, and allied health professionals, to identify their needs and expectations of the nursing consultation. Findings were integrated into the conceptualization process, which was conducted by the APN.

The content of the consultations, the target population, organizational framework conditions, personnel and structural resources, communication, financial reimbursement, evidence-based clinical practice, as well as internal and external networking and collaboration have been described in a concept. Possible challenges were identified, and supporting factors were presented. The nurse-led consultations are scheduled to start in May 2024, initially focusing on three topics.

All stakeholders recognize the need and advantages of nurse-led consultations. However, primary obstacle lies in financial reimbursement, as there is currently no legal framework for it. To address other obstacles, strategies have been identified. These include fostering ongoing dialogue about the project within the practice and engaging with external specialists. The consultations aim to be continually refined and broadened with new topics. A database will be established for evaluation and monitoring purposes.

HPR 2

Evaluation of usability and feasibility and acceptance of the digital training diary for individuals with axSpA

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Background: The Swiss ankylosing spondylitis association aims to implement exercise recommendations for individuals with axial spondyloarthritis (axSpA). A digital training diary (Trainingslog) was developed to promote physical activity (PA) through self-monitoring and feedback and be used for PA counselling. Usability is considered a key factor for the acceptance and use of a mobile health intervention and is defined in terms of user performance and satisfaction and acceptance in terms of product usage. Feasibility indicates the extent to

which an innovation can be successfully used or implemented in a particular organisation or environment. The quality of the mobile Health Intervention, as well as the adherence of the end-users is essentially influenced by the knowledge of usability, feasibility and acceptance of the Trainingslog.

Objective: To evaluate usability, feasibility and acceptance of the Trainingslog among individuals with axSpA and their physiotherapists (PTs) and to provide recommendations for further development.

Methods: A mixed-methods design was performed among the potential end-users of the Trainingslog. Data were collected through the questionnaires System Usability Scale (SUS, 0-100 scale) and user version of the Mobile App Rating Scale (uMARS, 5 point scale), number of training entries and semi-structured online focus groups or individual interviews.

Results: A total of 11 PTs and 10 individuals with axSpA participated. The quantitative data showed mean SUS scores for usability of: 82.5 (SD 21.76) for PTs and 77.0 (SD 9.34) for individuals with axSpA, and mean uMARS sector B scores for feasibility of: 4.2 (SD 0.49) for PTs and individuals with axSpA: 4.1 (SD 0.38). Acceptance was given according to the results of the uMARS (Sector E and F mean score >3 in both groups), but lower than expected agreement of the training entries (matching training entries in the Trainingslog and paper diary: 59.86%). The result of the qualitative data analysis revealed good usability and feasibility, but lower acceptance, which is mainly due to the web-based link instead of an app version.

Conclusion: The Trainingslog exhibits good usability and feasibility among individuals. Therefore, it shows potential to be used by PTs in PA counselling or as self-monitoring tool for individuals with axSpA. However, to increase acceptance, it is recommended to provide the Trainingslog in an app-based version and implement other suggestions for improvement.

HPR 3

Empowering self-management among male gout patients: a qualitative descriptive analysis

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Gout, a crystalline arthropathy is caused by hyperuricemia. Its prevalence has doubled in the last 15 years in Western countries and Oceania affecting up to 7.6% of the population, with 80% of patients being men.

Although a significant knowledge for the treatment of gout is available, patients receive suboptimal care. General practitioners often struggle to diagnose and educate patients about gout, leading to poor adherence to treatment and increased risk of co-morbidities. However, when Advanced Practice Nurses carry out medication education, patient adherence increases.

Diet contributes 12% to the development of gout while weight loss and physical activity are critical in managing potential co-morbidities. There is a literature gap as to what knowledge patients need about diet and lifestyle changes to self-manage their disease. highlighting the need for strategies to empower patients to manage their diet and lifestyle.

The research project explored the knowledge of male gout patients in relation to self-management support and provided recommendations for APNs to support these patients in managing their condition, particularly through dietary and lifestyle changes.

A qualitative structured content analysis was conducted and semi-structured interviews with male gout patients.

The results demonstrate patients received little support in self-managing their gout. Misconceptions about diet and alcohol were common. Knowledge about other lifestyle factors such as fluid intake, body weight and exercise was also vague. Also, patients expressed interest in alternative therapy methods and emphasised the importance of receiving written information about the disease. They attached great importance to specialist counselling to better understand the pathophysiology of the disease as well as the benefits and side effects of medication.

This study shows that gout patients need more information about how to manage their condition and highlights the need for advice from an APN. Consequently, it is recommended that APNs provide accurate and detailed information about diet and alcohol consumption, including lifestyle changes such as fluid intake, body weight and exercise. Written documentation of the issues discussed should be provided. And, where appropriate, alternative methods such as uric acid-lowering teas should be emphasised.

HPR 4

Patients' Perspective on Strengths and Weaknesses of the Bern Ambulatory Interprofessional Rehabilitation

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Background: The Bern Ambulatory Interprofessional Rehabilitation (BAI-Reha) is a three-month rehabilitation program for patients with chronic musculoskeletal pain. Patients provided written feedback on their experiences when they completed the program. Thus, the aim of this study is to analyse patients' experiences of the BAI-Reha. This leads to the primary research question: What strengths and weaknesses (including suggestions for change) do participants report at the end of the program? Secondly, we are interested in determining the frequencies of the topics mentioned.

Method: Participants received a feedback form at the end of the program with questions regarding strengths and weaknesses (including suggestions for change). To analyse the data we used a mixed method approach. The qualitative content analysis included inductive coding to determine main categories and themes. For the quantitative analysis, we conducted a frequency analysis in Microsoft Excel.

Results: We analysed 132 feedback forms with a total of 776 comments (421 strengths, 355 weaknesses). The most frequently mentioned strengths of the program were components of the medical-therapeutic content (166), followed by humanity and competence (124), the framework of the program (111), developed strategies (55), the positive peer support (35), and progress and positive personal outcomes (29). Participants frequently reported quantity, structure or missing content (161), organization (128), and medical-therapeutic content of the program (54) as weaknesses.

Conclusion: Feedback from participants supports the framework of the program with the aspects of versatility/holism, interprofessional collaboration and individual customisation. The organisation was often criticised, which reflects the challenge of planning an ambulatory program in a hospital setting. The results emphasize the importance of human qualities and the

value of motivated and competent health professionals. A major strength is the positive peer support in the group. Participants reported that the medical-therapeutic content of the program was significantly more often a strength rather than a weakness. Overall, participants suggested more often that the frequency/duration of therapies should be increased rather than reduced, even if they sometimes felt overwhelmed by the program. Thus, we interpret the overload in terms of information and physical demands as too much content in the beginning rather than too much content in the total program.

HPR 5

The implementation of exercise and education as first-line interventions for osteoarthritis and low back pain in Switzerland

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Introduction: International clinical guidelines for hip and knee osteoarthritis (OA) and for persistent or recurrent low back pain (LBP) management recommend exercise and education as first-line interventions. The GLA:D (Good Life with osteoArthritis in Denmark) initiative translates these guidelines into standardized but individualized programmes (GLA:D-OA and GLA:D-Back), which are implemented in clinical practice internationally provide high value care.

Methods: In Switzerland, the GLA:D programmes have been systematically implemented since 2019. The three core elements of GLA:D-OA and GLA:D-Back are 1) certification of physiotherapists (PTs) for uniformly providing the GLA:D programmes within their institution; 2) programmes for persons with hip and knee OA or LBP, consisting of four individual sessions and 14 group sessions (two patient education sessions and 12 supervised training sessions); 3) collection of all assessment and questionnaire data by PTs and patients in a national registry at entry, after completion, after 6 months (LBP only) and after 1 year. The data are analysed annually as part of the quality monitoring.

Results: So far, a total of 1056 GLA:D-certified PTs for OA and 508 PTs for LBP treated a total of 7575 hip and knee OA and 1024 LBP patients allover Switzerland. After intervention, the 3942 knee OA and 1084 hip OA patients with complete data showed improvements in pain of 25% and 22%, walking speed of 14% and 12%, quality of life of 23% and 16%, and pain medication use of 23% and 18%, respectively, all results were sustained after one year. The 533 LBP patients with complete data improved by 26% in pain intensity, 26% in pain medication consumption, 17% in physical function, 17% in fear of physical activity and 25% decrease in absence days. These improvements were sustained after six and even 12 months.

Conclusion(s): These evaluations showed that participants of the standardized, individually adapted, and evidence-based GLA:D programmes achieved substantial improvements after participation and in long-term evaluations. The successful long-term outcomes point out the importance of exercise and education in hip and knee OA and LBP and make an important contribution to best practice. The number of participating patients is increasing, however more effort and systematic implementation strategies are necessary to further and successfully implement the GLA:D programmes in the Swiss health care system.

HPR 6

Knowledge through images

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The exchange of information has never been greater than it is today. “Information design” explains a wide variety of content in the shortest possible time and combines several images with few words. This is because images have the power to simplify and visualise complex issues. We utilise this advantage on our ward at the Clinic for Rheumatology. Today’s world demands that information is easy to find, easy to understand and easy to access. Every nurse has to prepare efficiently for newly prescribed intravenous therapies. What has been, learned must be retrievable and refreshed in the shortest possible time. In the broadest sense, “information design” refers to the selection, organisation and preparation of information. The aim is to visualise even complex content as effectively and appropriately as possible for the specific group in mind, in order to enable the viewer to understand it quickly and easily.

With this in mind, the complex processes for the intravenous administration of various medications on the ward of the Clinic for Rheumatology were visualised. The aim of “information design” was used to simplify complex knowledge, increase quality standards, convey safety to users and carry out intravenous therapy applications in accordance with the standards. We also utilise today’s ways of learning. “Information design” is already used as part of the visual culture in many different areas. Nurses are used to using graphics to inform and orientate themselves. The simplified illustration of intravenous therapy application is intended to stimulate a thinking process. Quantities, rates and speeds are deliberately omitted. The schematic representation of intravenous therapy has been prepared in such a way that it is intuitively readable, but does not contain any information that would allow the therapy to be carried out without a specific prescription. The correct prescription and a corresponding guideline for administering the therapy must be provided. By implementing the images, the nursing team exchanges information about the intravenous therapy application more intensively. This increased safety during the administration and removed any doubts.

The quality and efficiency of the intravenous therapy application increased. The users reported feeling more confident, being able to inform themselves more efficiently and thus providing a higher quality of care to patients.

INDUSTRY

IP 1

Effect of Benralizumab versus Mepolizumab on Reduction in Oral Glucocorticoid Use in Patients with Eosinophilic Granulomatosis with Polyangiitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is characterised by asthma, hypereosinophilia, and vasculitis. Oral glucocorticoids (OGCs) and other immunosuppressive agents remain the cornerstone of treatment but have been associated with a wide range of adverse events, and relapses are common during tapering of OGCs.

Methods: MANDARA was a Phase 3, randomised, double-blind, 52-week, non-inferiority, head-to-head study (NCT04157348) evaluating the efficacy and safety of benralizumab 30 mg versus mepolizumab 300 mg sc Q4W, in adults with relapsing/refractory EGPA requiring ≥7.5 mg/day OGC (prednisolone/prednisone) ± immunosuppressive therapy. Investigators were encouraged to taper OGCs for patients with no active EGPA symptoms (BVAS = 0), according to standard practice and clinical judgement. Sustained reduction in OGC use was defined as achieving either 100% or ≥50% OGC reduction by Week 40 and maintaining reduction through to Week 52.

Results: 140 patients were randomised 1:1 to benralizumab (n = 70) or mepolizumab (n = 70); mean (standard deviation: SD) age was 52.3 (14.1) years and 60.0% were women. During Weeks 48–52, 41.4% of patients in the benralizumab group versus 25.8% in the mepolizumab group achieved complete withdrawal of OGC (difference: 15.69, 95% CI: 0.67, 30.71; p = 0.0406; Wechsler et al. NEJM 2024;310:911–21). More benralizumab- than mepolizumab-treated patients had sustained 100% reduction in OGC use (24.3% vs 10.0%; HR: 2.97 [95% CI: 1.26, 7.77]). Benralizumab- and mepolizumab-treated patients were able to taper off OGC regardless of antineutrophilic cytoplasmic antibody (ANCA)-status (benralizumab: 44.4% ANCA-positive vs 40.4% ANCA-negative; mepolizumab: 27.3% ANCA-positive vs 25.0% ANCA-negative) and immunosuppressive therapy (benralizumab: 38.5% with vs 43.2% without immunosuppressive use; mepolizumab: 29.2% with vs 23.9% without immunosuppressive use). A similar proportion of patients in both groups achieved sustained ≥50% reduction in OGC use (77.1% vs 70.0% in benralizumab vs mepolizumab groups; HR: 1.17 [95% CI: 0.79, 1.74]; p = 0.3852). Benralizumab-treated patients tapered OGCs faster than mepolizumab-treated patients and maintained reduction in dose through to Week 52.

Conclusions: Treatment with benralizumab or mepolizumab enabled reduction in OGC use in patients with EGPA. Compared with mepolizumab-treated patients, benralizumab-treated patients tapered OGCs faster and were more likely to fully eliminate use of OGC.

IP 2

Clinical Characteristics, Including History of Myocardial Infarction and Stroke, Among US PMO Women Initiating Treatment with Romosozumab and Other Anti-Osteoporosis Therapies

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Background: This ongoing FDA postmarketing requirement study (2020–24) assesses the impact of the boxed cardiovascular (CV) warning on romosozumab (Romo) treatment and informs feasibility of a future comparative safety study.

Methods: This retrospective study uses repeated analyses within five 1-year blocks since Romo approval (2019) and includes women (≥55 years) newly initiating Romo, denosumab (DMAb), intravenous zoledronate, parathyroid hormone (PTH) analogues or oral bisphosphonates. From data identified using Optum and Medicare databases, we compared baseline demographics and clinical characteristics (including myocardial infarction [MI] or stroke within 1 year before treatment initiation and history of CV, fracture and other CV risk factors) in patients initiating Romo vs other osteoporosis (OP) treatments (clinically significant difference = absolute standardised mean difference [SMD] >0.10). We also conducted propensity score matching (PSM) of clinical characteristics (referent Romo).

Results: From April 2019 to September 2021, we identified 16,475 Romo users (Optum 1,879; Medicare 14,596). The proportion of patients with a history of an MI or stroke was very low (0.1–0.2%) in both Optum and Medicare databases and was numerically lower in patients initiating Romo vs other OP treatments (all absolute SMDs <0.10). Patients initiating Romo vs other treatments (except DMAb) were older, and a higher proportion (except PTH users) had prior baseline healthcare utilisation and OP-related history (fractures, OP treatment). The proportion of patients with a history of other CV risk factors were similar between Romo and other treatment groups. Romo was most frequently administered by rheumatologists in the Medicare population (34.9%). All baseline clinical characteristics were balanced after PSM.

Conclusion: Romo-initiating patients were mostly older and had a greater history of fractures and OP treatment, similar history of hypertension, type II diabetes, arrhythmia, and smoking, and similarly low or numerically lower rates of MI or stroke before Romo initiation compared with patients initiating other OP treatments. These data suggest the FDA-required boxed CV warning continues to have its intended effect on patient selection.

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IP 3

Romosozumab in Denmark – A Registry Study on Osteoporosis Patients

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Background: Romosozumab was approved in the European Union in December 2019 for the treatment of severe osteoporosis (OP) in postmenopausal women at high risk of fracture and has been reimbursed in Denmark since September 2020. This study is the first to describe the profile of patients selected for romosozumab treatment in Denmark.

Methods: We performed a retrospective cohort study based on data from Danish administrative registries. The study population comprised female patients aged ≥50 receiving OP medication during the period September 2020 to October 2023.[1] The study included three cohorts: i) patients with severe OP treated with romosozumab, ii) patients with severe OP not treated with romosozumab, and iii) patients who did not have severe OP and were not treated with romosozumab. Patients were considered as having severe OP if they had sustained a fracture at any skeletal site in the three years before the index date (bone mineral density data were not available in the dataset). The characteristics investigated in the three cohorts included: age, index treatment, comorbidities, OP treatment history, dispensing of drugs that increase risk of falling and fracture, fracture history, and use of glucocorticoids.

Results: Overall, 149,395 patients were included. Patients treated with romosozumab were generally younger, had lower instances of comorbidities (cardiovascular disease; diabetes; malignancy) and glucocorticoid use than patients not treated with romosozumab. Of the 622 patients treated with romosozumab, 277 (44.5%) had not received any prior treatment for OP.

Conclusions: This study provides insight into the patterns and influencing factors of romosozumab use in routine clinical practice in Denmark. Patients treated with romosozumab were younger, had lower prevalence of comorbidities and instances of glucocorticoid use.

Footnotes: [1] Identified by prescription data up to and including August 2023, and hospital registry data up to and including October 2023

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IP 4

Complete Remission in Eosinophilic Granulomatosis with Polyangiitis in the MANDARA Trial of Benralizumab versus Mepolizumab

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Background: In patients with eosinophilic granulomatosis with polyangiitis (EGPA) there is a need to minimise long-term use of oral glucocorticoids (OGCs) to avoid associated adverse outcomes, while sustaining remission and avoiding relapse. MANDARA was a Phase 3, randomised, double-blind, parallel-group, multicentre study (NCT04157348) of benralizumab 1x30 mg versus mepolizumab 3x100 mg, subcutaneously every 4 weeks in patients with relapsing/refractory EGPA receiving standard of care. Non-inferiority was demonstrated for remission (Birmingham Vasculitis Activity Score [BVAS] = 0 and OGC ≤4 mg/day), at both Weeks 36 and 48 (primary endpoint).

Methods: Post-hoc analyses of MANDARA assessed the proportion of patients achieving a more stringent definition of complete remission: BVAS = 0 and OGC dose = 0 mg/day at both Weeks 36 and 48 and being relapse-free. Remission was considered sustained if criteria were first met by Week 40 and maintained until the end of the 52-week double-blind period. Investigators were encouraged to taper OGCs for patients who reached BVAS = 0, according to standard practice and clinical judgement.

Results: 140 patients received benralizumab (n = 70) or mepolizumab (n = 70). Adjusted rates of remission at both Weeks 36 and 48 were 59.2% with benralizumab versus 56.5% with mepolizumab (difference: 2.71 [95% CI: –12.54, 17.96]; p = 0.7278; Wechsler et al. N Engl J Med. 2024;390:911–921). Adjusted rates of complete remission at both Weeks 36 and 48 were 23.5% versus 11.1% (difference: 12.47 [95% CI: 0.46, 24.48]; p = 0.0418) in the benralizumab and mepolizumab groups, respectively. Sustained remission was achieved by 60.0% and 55.7% of patients (HR: 1.30 [95% CI: 0.84, 2.04]; p = 0.5874) in the benralizumab and mepolizumab groups; and sustained complete remission was achieved by 24.3% and 14.3% patients (HR: 2.10 [95% CI: 0.97, 4.84]; p = 0.1228), respectively.

Conclusions: Patients with EGPA receiving benralizumab and mepolizumab achieve similar remission rates when using a definition of OGC ≤4 mg/day, and numerically higher rates are seen for benralizumab versus mepolizumab using the more stringent definition of complete remission that included OGC = 0 mg/day and being relapse-free. These data highlight the possibility of achieving sustained treatment goals for patients with EGPA receiving anti-IL-5/Rα therapy that include full tapering of OGCs and avoiding relapses.

Funding: AstraZeneca.

IP 5

Sustained improvements with bimekizumab in patient-reported symptoms of axial spondyloarthritis: 2-year results from two phase 3 studies

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Background: In BE MOBILE 1 and 2 (NCT03928704; NCT03928743), bimekizumab (BKZ) demonstrated sustained improvements in key symptoms to 52 weeks (wks) in non-radiographic (nr-)axial spondyloarthritis (axSpA) and radiographic (r-)axSpA patients (pts), respectively.1

Methods: Pts randomised to BKZ 160mg every 4wks (Q4W) or placebo (PBO); from Wk16 all received BKZ 160mg Q4W. Wk52 completers of either study could enter BE MOVING (NCT04436640; open-label extension [OLE]). We report mean values and change from baseline (CfB) in total and nocturnal spinal pain, morning stiffness (mean of Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] questions [Q]5 and Q6) and fatigue (BASDAI Q1 and Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue scores) to Wk104 (multiple imputation [MI]). We report pt proportions achieving total and nocturnal spinal pain scores <2, indicating minimal (score = 1) or no (score = 0) back pain, and <4, based on study inclusion criteria of spinal pain ≥4 according to BASDAI Q2, as well as FACIT-Fatigue responders (≥8-point increase in pts with baseline score ≤44) to Wk104 (non-responder imputation [NRI]). Data are pooled for all randomised pts with nr-axSpA and r-axSpA in BE MOBILE 1 and 2.

Results: Of the 254 nr-axSpA/332 r-axSpA pts randomised to BKZ or PBO in the feeder studies, 494 (84.3%) entered OLE. By Jul-2023, 456 pts completed Wk104. Baseline symptoms were comparable between treatment groups (mean scores of 7.2/6.7, 6.8 and 30.9 for total/nocturnal spinal pain, morning stiffness and FACIT-Fatigue scores, respectively). Improvements at Wk52 sustained to Wk104 for spinal pain and morning stiffness scores (CfB: –4.2 Wk52; –4.3 Wk104). Results were similar for BASDAI fatigue (CfB: –3.1 Wk52; –3.4 Wk104). Improved FACIT-Fatigue scores were sustained throughout OLE (CfB:+9.9 at Wk52 and Wk104). From Wk52–104, >50% patients had total (Wk52: 56.0; Wk104: 53.9) and nocturnal (Wk52: 62.5; Wk104: 57.3) spinal pain scores <4; >25% and >35% had scores <2, respectively (N = 586). 55.8% and 52.3% were FACIT-Fatigue responders at Wk52/Wk104, respectively (N = 520). Results were similar across nr-/r-axSpA pts.

Conclusions: Results from 2yrs' BKZ treatment demonstrated sustained improvements in spinal pain, morning stiffness and fatigue in nr-/r-axSpA pts, emphasising longer-term BKZ benefit on clinical symptoms.

Funding: UCB Pharma. Editorial services: Costello Medical.

Previously submitted to EULAR 2024.

Reference

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IP 6

Impact of bimekizumab on MRI inflammatory and structural lesions in the sacroiliac joints of patients with axial spondyloarthritis: 52-week results and post hoc analyses from the BE MOBILE 1 and 2 phase 3 studies

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Background: We report impact of bimekizumab (BKZ) on MRI inflammatory and structural lesions in sacroiliac joints (SIJ) in patients (pts) with non-radiographic/radiographic axial spondylarthritis (nr-/r-axSpA) from the phase 3 BE MOBILE 1 and 2 studies.1

Methods: In BE MOBILE 1 (nr-axSpA; NCT03928704) and 2 (r-axSpA; NCT03928743) pts were randomised to BKZ 160mg every 4 weeks (wks; Q4W) or placebo; all received BKZ Q4W from Wk16–52. Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ inflammation scores and SPARCC SIJ Structural Score (SSS) were assessed at baseline, Wk16 and Wk52 in MRI sub-studies. MRIs were assessed centrally by two independent experts (disagreements adjudicated). Inflammatory and structural lesions were assessed by different readers. All readers were blinded to timepoint/clinical data; structural lesions were analysed post hoc. Observed case data are reported.

Results: 60% (152/254) and 42% (139/332) of pts with nr-/r-axSpA enrolled in MRI sub-studies. 76% (115/152) and 78% (109/139) had valid SPARCC inflammation assessments at all timepoints, respectively, and 84% (128/152) and 83% (116/139) of pts had valid SPARCC SSS assessments at all timepoints. For continuous BKZ pts, reductions in SPARCC inflammation at Wk16 (mean absolute scores: 1.6 [BE MOBILE 1], 1.2 [BE MOBILE 2]) were maintained to Wk52 (1.0 and 0.9 in BE MOBILE 1/2, respectively); pts switching from placebo to BKZ at Wk16 reached similar Wk52 levels as continuous-BKZ pts (1.8 and 0.9 in BE MOBILE 1/2, respectively). Reductions in SPARCC SSS for erosions were observed with BKZ versus placebo at Wk16: –0.9 vs 0.0 CfB in BE MOBILE 1 and –1.0 vs 0.1 in BE MOBILE 2. For backfill, increase in mean Wk16 CfB was 0.3 vs 0.0 in BE MOBILE 1 and 0.4 vs 0.0 in BE MOBILE 2. For fat, 0.3 vs 0.2 in BE MOBILE 1 and 0.6 vs 0.0 in BE MOBILE 2. Further improvements were seen to Wk52 in the continuous-BKZ group; similar changes were observed in placebo-switchers. No SPARCC SSS change for ankylosis was observed in pts with nr-axSpA.

Conclusions: BKZ improved MRI inflammation, reduced erosions and increased backfill and fat in the SIJ of pts with axSpA, which may suggest evidence of tissue repair.

Funding: UCB Pharma. Editorial services: Costello Medical.

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Reference

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IP 7

Long-term safety and tolerability of bimekizumab in patients with axial spondyloarthritis and psoriatic arthritis: Results from pooled phase 2b/3 studies

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Background: Here, we present long-term pooled safety data for bimekizumab (BKZ) in axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) patient (pt) populations.

Methods: We report two pooled analyses, each comprising three phase 2b/3 trials and their open-label extensions (OLEs) in pts with non-radiographic (nr)- and radiographic (r)-axSpA, and PsA, respectively.[1–4] Report number, proportion and/or exposure-adjusted incidence rates per 100 pt-years (EAIR/100 PY) of treatment-emergent adverse events (TEAEs) for pts who received ≥1 BKZ 160mg dose every four weeks. Data reported to Jul-22 data-cut.

Results: axSpA/PsA safety pools included 848 pts (2034.4 PY) and 1,407 pts (2590.8 PY), respectively. Most frequent TEAEs were nasopharyngitis (axSpA: 17.2%; PsA: 12.8%), SARS-CoV-2 infection (axSpA: 15.7%; PsA: 14.3%) and upper respiratory tract infection (axSpA: 11.1%; PsA: 9.7%).

161 (19.0%) axSpA pts (EAIR/100 PY: 9.2) and 214 (15.2%) PsA pts (EAIR/100 PY: 9.2) had fungal infections, 19 of which discontinued (7 axSpA [0.8%], 12 PsA [0.9%]); no systemic fungal infections. Most were oral; vast majority mild to moderate (axSpA: 162 [99.4%]; PsA: 231 [99.6%]). Two pts had severe oral fungal infections (axSpA: 1 [0.1%]; PsA: 1 [0.1%]); both resolved with treatment. Candida fungal infection rates were similar in axSpA and PsA. Serious infections/infestations found in 29 (3.4%) axSpA pts (EAIR/100 PY: 1.5) and 30 (2.1%) PsA pts (EAIR/100 PY: 1.2). One serious fungal infection (oropharyngeal candidiasis) reported (PsA: 1 [<0.1%]; resolved with treatment). Adjudicated IBD (definite/probable) occurred in 16 axSpA pts (EAIR/100 PY: 0.8) and 7 PsA pts (EAIR/100 PY: 0.3). Uveitis found in 25 axSpA pts (EAIR/100 PY: 1.2); none in PsA. Adjudicated major adverse cardiovascular events occurred in 4 axSpA pts (EAIR/100 PY: 0.2) and 10 PsA pts (EAIR/100 PY: 0.4). Five pts experienced adjudicated suicidal ideation/behaviour events (3 axSpA(EAIR/100 PY: 0.1); 2 PsA(EAIR/100 PY: 0.1). No cases of suicide or active tuberculosis.

Conclusions: The long-term safety profile of BKZ is consistent with prior axSpA/PsA studies.1 As expected, oral candidiasis was among the safety signals reported.

Funding: UCB Pharma. Editorial services: Costello Medical.

Previously presented at ACR 2023.

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IP 8

Bimekizumab-treated patients with active psoriatic arthritis showed sustained achievement of minimal disease activity and remission: Up to 2-year results from two phase 3 studies

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease with multiple affected domains.1 We assess bimekizumab (BKZ) efficacy using composite outcomes, such as minimal disease activity (MDA) and remission, in PsA patients (pts).

Methods: BE OPTIMAL and BE COMPLETE (placebo [PBO]-controlled to Week [Wk]16) assessed BKZ 160mg every 4 wks (Q4W) in bDMARD-naïve PsA pts or pts with inadequate response/intolerance to TNF inhibitors (TNFi-IR), respectively. BE OPTIMAL had an adalimumab (ADA) 40mg Q2W reference arm. PBO pts switched to BKZ (PBO/BKZ) at Wk16. BE OPTIMAL Wk52/BE COMPLETE Wk16 completers could enter BE VITAL (open-label extension); all received BKZ. Pt populations referred to by starting study name hereafter. Endpoints include MDA and very low disease activity (VLDA) responses/components, Disease Activity Index for PsA (DAPSA) remission or LDA (REM ≤4; REM+LDA ≤14) responses and DAPSA change from baseline (CfB). Data reported to BE OPTIMAL Wk104/BE COMPLETE Wk100. Non-responder/worst-category imputation used for missing data.

Results: 710/852 (83.3%) and 322/400 (80.5%) pts completed Wk104/Wk100 of BE OPTIMAL/BE COMPLETE, respectively. Baseline MDA components were comparable between treatment groups in trials. In BKZ-randomised pts, Wk52 MDA achievement (bDMARD-naïve 54.8%; TNFi-IR 46.4%) was sustained to Wk104/100 (bDMARD-naïve 52.4%; TNFi-IR 44.9%). PBO/BKZ pts' MDA achievement was sustained Wk52 (53.7%)–Wk104 (49.8%) in bDMARD-naïve pts and Wk52 (33.1%)–Wk100 (46.6%) in TNFi-IR pts. bDMARD-naïve ADA/BKZ pts' MDA achievement was sustained Wk52 (52.9%)–Wk104 (50.7%). Trends were similar at Wk104/100 for achievement of DAPSA REM+LDA (52.9% [Wk104; bDMARD-naïve]; 46.1% [Wk100; TNFi-IR]; all BKZ-randomised) and VLDA. Mean DAPSA scores were sustained Wk52–Wk104/100 in BKZ-randomised pts (bDMARD-naïve: –30.4 [Wk52 and Wk104]; TNFi-IR: –33.8 [Wk52] vs –35.9 [Wk100] CfB). To Wk104/100, BKZ led to large improvements in most MDA components (all treatment arms; both trials), including clinical (swollen/tender joint count; skin) and pt-reported components (pain; physical function).

Conclusions: BKZ led to sustained MDA and DAPSA REM+LDA responses to 2 years, regardless of prior bDMARD use. We saw improvements across all pt-reported and most clinical MDA components, especially in joint/skin outcomes.

Funding: UCB Pharma. Editorial support: Costello Medical.

Previously submitted to EULAR 2024.

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IP 9

Bimekizumab impact on core Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) domains for patients with psoriatic arthritis: 52-week results from four phase 3 studies

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Background: The Group for Research and Assessment of Psoriasis and PsA (GRAPPA) domain-based treatment recommendations for psoriatic arthritis (PsA) focus on six key domains: peripheral arthritis, axial disease, enthesitis, dactylitis, skin psoriasis and nail psoriasis, and PsA-related conditions: uveitis and inflammatory bowel disease (IBD).1 Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated superior clinical efficacy vs placebo (PBO) to Week (Wk)16 in phase 3 clinical trials of patients (pts) with PsA.2,3 Here, we show BKZ efficacy across GRAPPA core domains to Wk52 for PsA pts, with axial domain outcomes for axial spondyloarthritis (axSpA) pts.

Methods: Pts were randomised to BKZ 160mg or PBO every 4 wks (Q4W) in BE OPTIMAL (NCT03895203; biologic DMARD-naïve PsA), BE COMPLETE (NCT03896581; TNFi-inadequate response [TNFi-IR] PsA), BE MOBILE 1 (NCT03928704; non-radiographic axSpA) and 2 (NCT03928743; radiographic axSpA). From Wk16, PBO-randomised pts received BKZ 160mg Q4W to Wk 52 (PBO/BKZ). BE COMPLETE Wk16 completers could enter BE VITAL (NCT04009499; open-label extension). Outcomes are reported by GRAPPA domain. Missing data: non-responder and multiple imputation, or observed case.

Results: Wk52 completion was high (BE OPTIMAL: 770/852 [90.4%], BE COMPLETE: 347/400 [86.8%], BE MOBILE 1: 220/254 [86.6%], BE MOBILE 2: 298/332 [89.8%]). Across all GRAPPA domains, Wk16 improvements were sustained at Wk52 in BKZ-treated pts across all studies. Individual domain responses were generally consistent between bDMARD-naïve and TNFi-IR pts. BE MOBILE 1/2 demonstrated BKZ efficacy in axSpA pts and suggested efficacy for axial disease in PsA. Wk52 responses were generally consistent between BKZ and PBO/BKZ pts. To Wk52, there were no uveitis cases (BE OPTIMAL; BE COMPLETE). Two (0.2%) pts in BE OPTIMAL had definite adjudicated IBD; none in BE COMPLETE.

Conclusions: BKZ treatment resulted in robust, sustained improvements across GRAPPA domains with low rates of IBD and no uveitis to Wk52 for bDMARD-naïve/TNFi-IR PsA pts; results from axSpA pts support efficacy in the axial domain.

Study Funding: UCB Pharma. Editorial services: Costello Medical.

Previously presented at ACR 2023.

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IP 10

Efficacy of bimekizumab in patients with axial spondyloarthritis with shorter versus longer symptom duration: 1-year results from two phase 3 studies

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Background: Bimekizumab (BKZ) has shown efficacy to Week (Wk)52 in axial spondyloarthritis (axSpA) patients (pts) in BE MOBILE 1/2.1,2 BKZ effect in pts with early symptom duration has not yet been assessed.

Methods: BE MOBILE 1 (non-radiographic axSpA; NCT03928704) and 2 (radiographic axSpA; NCT03928743) randomised pts to BKZ 160mg every 4 weeks or placebo (PBO); all received BKZ Wk16–52. We analysed ASAS40 (non-responder imputation), ASDAS <2.1, mean BASDAI change from baseline (CfB; both multiple imputation) and mean MRI SIJ Spondyloarthritis Research Consortium of Canada (SPARCC) score (observed case; MRI sub-study pts) for duration of symptoms (DoS) ≤5/>5 years to Wk52. Wk16 relative odds ratios (ASAS40, ASDAS <2.1) and relative differences (RD; BASDAI CfB) were calculated (sample size-permitting). Due to small sample size, only BE MOBILE 1 DoS ≤2/>2 years clinical efficacy outcomes (early axSpA consensus definition)3 were analysed.

Results: BKZ showed better outcomes vs PBO at Wk16, regardless of DoS. Outcomes were sustained/improved in DoS subgroups to Wk52. Wk16 ASAS40 and ASDAS <2.1 responses were numerically higher in DoS ≤5 vs DoS >5 BKZ-treated pts (ASAS40: 56.7% vs 39.7% [BE MOBILE 1], 53.8% vs 42.9 [BE MOBILE 2]); we found no difference between DoS ≤5/>5 (BE MOBILE 1/2) or DoS ≤2/>2 (BE MOBILE 1). We found no difference in Wk16 mean BASDAI CfB between DoS ≤5/>5 or DoS ≤2/>2 in BE MOBILE 1, but greater BASDAI improvement in DoS ≤5 vs >5 in BE MOBILE 2. Baseline MRI SIJ SPARCC scores indicated greater SIJ inflammation in DoS ≤5 vs >5. BKZ treatment led to lower mean Wk16 MRI SIJ SPARCC scores in both DoS subgroups, and no significant difference between DoS ≤5/>5 vs PBO in BE MOBILE 1 (RD [95% confidence interval]: −3.10 [−8.09, 1.90]). Mean Wk16 MRI SIJ SPARCC scores of BKZ-treated pts (BE MOBILE 1: DoS ≤5: 1.8 [n = 36], DoS >5: 2.1 [n = 42]; BE MOBILE 2: DoS ≤5: 1.2 [n = 15], DoS >5: 1.5 [n = 66]) remained low to Wk52, indicating inflammation resolution, regardless of DoS.

Conclusions: No significant difference in short-term outcomes between shorter vs longer DoS pts was seen. Shorter DoS pts had greater MRI SIJ inflammation pre-treatment, demonstrating importance of targeting inflammation earlier.

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IP 11

Effectiveness and safety of mono-or combination therapy with Sarilumab in rheumatoid arthritis: 24-month, single-arm, German PROSARA study

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Background: Sarilumab, an interleukin-6 receptor inhibitor, has demonstrated treatment effectiveness in rheumatoid arthritis (RA) in routine care1,2, but only a few real-world long-term studies are available. This study assessed the effectiveness, safety and, patient-reported outcomes of sarilumab in daily clinical practice in patients with RA over a prolonged observation period.

Methods: This prospective, non-interventional, open label, multicentre, single-arm study (PROSARA) was conducted from March 2018 to February 2023 in Germany. Adult patients with moderate to severe RA, with prior RA therapy and treated for the first time with sarilumab (mono/combination therapy) (150/200 mg Q2W) were enrolled. Clinical effectiveness of sarilumab was assessed at 12 and 24 months using clinical disease activity index (CDAI), simplified disease activity index (SDAI), disease activity score in 28 joints (DAS28), and health assessment questionnaire disability index (HAQ-DI) score. Safety was assessed by frequency of adverse event, serious adverse event (SAE), adverse drug reaction. All analyses for patients initiating sarilumab close to baseline (±14 days) were presented to ensure meaningful interpretation due to potential deviation in sarilumab initiation from the date of baseline visit.

Results: A total of 584 patients (76.9% female, mean±SD age: 58.6 ± 11.5 years, median time since diagnosis: 91 months [~7.6 years; IQR: 39–187]) were included. At baseline, 54.5% of patients started sarilumab as monotherapy, 30.7% received sarilumab in combination with csDMARD, data for the remaining patients unknown. There was a clinically relevant improvement in disease activity. At 24 months, most patients were in DAS28 remission (DAS28CRP; 61.4% and DAS28ESR; 72.4%), whereas 28.4% and 28.0% of patients were in CDAI and SDAI remission, respectively. DAS28 remission was not significantly associated with prior RA treatment (except for DAS28CRP remission for TNFi). The HAQ-DI score was improved after 12 and 24 months of therapy onset. Most frequent SAEs were musculoskeletal and connective tissue disorders (3.9%), surgical and medical procedures (2.6%), and infections and infestations (2.4%).

Conclusion: In daily clinical practice in Germany, sarilumab showed sustained improvement in various effectiveness parameters in RA with no new safety signals.

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IP 12

Clinical and Economic Burden of Polymyalgia Rheumatica in Patients with an Inadequate Response to Glucocorticoids or unable to taper Glucocorticoids in a Real-World Setting

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Background: Nearly 50% of PMR patients experience flares upon GC taper/discontinuation, with a significant burden of continuing GC, necessitating GC-sparing therapies.

Objective: To assess clinical and economic outcomes of continuing GC in PMR with an inadequate response (IR) to GC/GC-taper.

Methods: A new-onset PMR cohort from Medicare claims identified from 10/1/2016 to 12/31/2019 included patients age ≥50, without PMR/ giant cell arteritis history and 1) ≥1 inpatient or ≥2 outpatient claims for PMR ≥30 days (D) to <365D apart, 2) GC initiation 7.5–25mg/D <30D after 1st inpatient or from 1st outpatient code to 30D after 2nd code with GC dose ≥200mg in 1st ≤30D GC use ≥4 months (Mo), 3) enrollment ≥1 year before index, defined as latter of meeting diagnosis/GC criteria, and 4) ≥2 years follow-up. Patients with seropositive RA/other rheumatic disease/organ transplant/multiple sclerosis/malignancy treatment/ conventional immunomodulatory drugs or IL-6 receptor inhibitor during baseline were excluded. Patients were split into 2 groups 1) IR to GC/GC taper: presumed flare if GC dose ≥7.5mg/D at 6 Mo or GC use >12 Mo or relapse if GC used after discontinuation (>60D gap); 2) non-IR to GC/GC taper. GC-related adverse events (GC-AEs) incidence rates and all-cause healthcare resource utilization (HCRU) cost were reported from 6 Mo after index over 12 Mo intervals. For GC-AEs incidence rate, only the 1st event was counted except hospitalized infections and fractures. Poisson methods were used to estimate event rates/100 patient-years (PY). Subgroup analysis of the IR group estimated outcomes by cumulative GC dose quartiles.

Results: This analysis included 6054 PMR patients (65.4% females; mean age: 77.1 years). All-cause HCRU cost was higher in IR vs non-IR (mean difference US Dollar: 4781, 6051, 4168, and 6461 at >6–18, >18–30, >30–42, and >42–54 Mo) and most GC-AE incidences were higher in the IR vs non-IR group (i.e., hospitalized infections events/100 PY: 26 vs 17, 25 vs 13, 19 vs 13 and 19 vs 15 at >6–18, >18–30, >30–42, and >42–54 Mo). In the IR group, all-cause HCRU cost and most GC-AEs decreased over time and exhibited a GC dose-response relationship with most outcomes.

Conclusion: The clinical and economic burden of persistent GC use in PMR patients unable to taper GC or who relapse is significant, lasting even after discontinuation which emphasize the need for GC-sparing therapies to mitigate the long-term impact of GCs.

IP 13

Effectiveness of IL-6 Receptor Inhibitors Versus Methotrexate or any Conventional Immunomodulators in Patients with Steroid Refractory Polymyalgia Rheumatica

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Background: A retrospective observational study (based on Medicare data) reported the effectiveness of interleukin-6 receptor inhibitors (IL-6Ri) vs conventional synthetic immunomodulators (csIM) in glucocorticoid (GC)-refractory polymyalgia rheumatica (PMR) (Curtis JR et al, AMCP 2023). Despite direct/propensity score match, residual differences remained, prompting adjustment to the matching and exclusion criteria.

Methods: This analysis included adults ≥50 years old, with 1 inpatient/2 outpatient PMR Medicare claims (3/29/16–6/30/20). Patients were on ≤25mg GC, started IL-6Ri/csIM as 2nd/3rd line (2L/3L) therapy (index), and had 180-days-continuous enrolment prior-index (baseline). In the main cohort, age, sex, daily GC dose category, baseline GC dose category, and history of giant cell arteritis (GCA) were included as direct-match criteria. A post-hoc analysis compared IL-6Ri to methotrexate (MTX) (MTX subgroup). An additional cohort was created that excluded the GCA history (sensitivity cohort). The primary outcomes were time to GC discontinuation and minimal/no GC at 1-year using Cox-proportional hazard model.

Results: The main and sensitivity cohorts had 415 (203 MTX-subgroup) and 451 matched pairs, respectively. Significantly more IL-6Ri vs csIM/MTX patients discontinued GC or were on minimal/no GC at 1-year (P <0.05). Results were significant in the 2L/3L in main cohort for GC discontinuation (49.2% vs 37.4%, P = 0.022[2L]/45.2% vs 28.9%, P <0.001[3L]) and minimal/no GC (54.5% vs 41.2%, P = 0.010[2L]/47.4% vs 32.5%, P = 0.001[3L]), and sensitivity cohort. In MTX subgroup, results were significant only in 2L for GC discontinuation (49.4% vs 35.2%, P = 0.010[2L]/34.1% vs 36.6%, P = 0.817[3L]) and minimal/no GC (55.6% vs 38.9%, P = 0.003[2L]/36.6% vs 36.6%, P >0.999[3L]). Mean cumulative GC dose was lower with IL?6Ri vs csIM/MTX but difference was not significant. Time-to-event analyses favored IL-6Ri over csIM/MTX for GC discontinuation across all cohorts (HR [95%CI], main cohort:1.28[1.02-1.60], P = 0.031; sensitivity cohort:1.30[1.05-1.61], P = 0.018; MTX subgroup:1.29[0.95-1.75], P = 0.109). IL-6Ri vs csIM/MTX patients were significantly more likely to be on minimal/no GC in all cohorts at 1-year (HR [95%CI], main cohort:1.28[1.03-1.58], P = 0.025; sensitivity cohort:1.29[1.04-1.58], P = 0.025; MTX subgroup:1.41[1.05-1.89], P = 0.022).

Conclusion: IL-6Ri was a more effective steroid sparing agent than csIM/MTX. IL-6Ri has the potential to reduce cumulative GC exposure in PMR.

IP 14

Sarilumab in Patients with Relapsing Polymyalgia Rheumatica: A Phase 3, Multicenter, Randomized, Double Blind, Placebo Controlled Trial (SAPHYR)

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Background: SAPHYR study (NCT03600818) assessed the efficacy and safety of sarilumab (SAR), an interleukin-6 receptor inhibitor, with 14 week (W) glucocorticoid (GC)-taper in patients with GC-resistant Polymyalgia rheumatica (PMR) who flared on ≥7.5mg/day prednisone or equivalent.

Methods: Patients were randomized (1:1) to 52W SAR 200mg every 2W (Q2W)+14W GC taper (SAR arm) OR placebo Q2W+52W GC-taper (comparator arm). The primary endpoint included proportion of patients achieving sustained remission (SR) at W52, defined as remission by W12, absence of disease flare, C-reactive protein (CRP) normalization, and adherence to GC-taper, from W12 to W52.

Results: Between 10/2018 and 07/2020, 60 and 58 patients randomized to SAR and comparator. Demographics were balanced between arms; patients primarily female, Caucasian, median age ~70 years. Overall, 78 patients completed treatment (SAR n = 42; comparator n = 36). Primary reasons for treatment discontinuation were adverse events (AEs) (SAR n = 7; comparator n = 4) and lack of efficacy (SAR n = 4; comparator n = 9). SR rate was significantly higher in SAR vs comparator arm (28.3% vs 10.3%; P = 0.0193). Sensitivity analysis excluding CRP and ESR from SR definition was consistent with primary analysis (31.7% vs 13.8%; P = 0.0280). All SR components favored SAR. Patients in SAR vs comparator arm were 44% less likely to have a flare after achieving remission (16.7% vs 29.3%; hazard ratio 0.56; 95% CI 0.35-0.90; P = 0.0158). The comparator arm required more additional GCs vs SAR arm, mainly due to PMR flare (median difference in actual and expected cumulative dose 199.5mg vs 0.0mg; P = 0.0189). The cumulative GC-toxicity index scores numerically favored SAR. PMR activity scores improved in SAR vs comparator arm (LS mean −15.57 vs −10.27, nominal P = 0.0002). Patient reported outcome analyses (physical and mental health component scores, and disability index) favored SAR. Incidence of treatment-emergent AEs was numerically higher in SAR vs comparator arm (94.9% vs 84.5%) and included neutropenia (15.3%) and arthralgia (15.3%) in SAR arm, and insomnia (15.5%) in comparator arm. The frequency of serious AEs was higher in comparator arm vs SAR arm (20.7% vs 13.6%). No deaths were reported.

Conclusions: SAR+14W GC-taper demonstrated significant efficacy vs comparator arm in GC refractory PMR patients, including clinically meaningful improvement in quality of life. Safety was consistent with the known safety profile of SAR.

IP 15

Establishment of an immunocapture method for the separation of a rheumatoid arthritis-related CD90+ subpopulation of extracellular vesicles

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Extracellular vesicles (EVs) are cell-produced, small particles (30-1000nm) which were previously reported to contribute to the pathogenesis of various diseases including rheumatoid arthritis (RA). However, most studies are based on bulk analysis of EVs, neglecting the complexity of different EV subsets present in biofluids of patients. To investigate and characterize distinct EV subpopulations within a heterogeneous mix of EVs in RA, we established an immunocapture separation method based on magnetic, nano-sized beads targeting a relevant marker in RA synovial tissue. In this context CD90/THY1 was selected due to the reported contribution of CD90+ fibroblasts in RA synovitis.

Methods: EVs secreted from cultured synovial fibroblasts of arthritis patients (RA and OA) were isolated via size exclusion chromatography and subsequently characterized via TEM, NTA, NanoFCM and Western Blot (WB). The separation of a CD90+ population from the heterogenous EV population was performed with prototype anti-CD90 EV Isolation MicroBeads (Miltenyi). WB and mass-spectrometry based proteomics were applied to identify characteristics and differences between the two populations. Spiking of fibroblast-derived EVs in RA patient-derived synovial fluid was used to test the separation approach in more complex source material. A THP1 dual reporter assay exhibited first differences of synovial fluid-derived EVs between RA and OA.

Results: The presence of CD90 on EVs derived from cultured fibroblasts was shown by WB and NanoFCM. After magnetic bead-based separation of fibroblast-derived EVs, WB and proteomics confirmed the enrichment of CD90 in the CD90+ population. Both populations further exhibited distinct EV marker patterns with enriched Annexin-1 in CD90+ EVs and CD63 and Flotillin-1 in the CD90- population. Spiked CD90+ EVs were successfully retrieved from synovial fluid demonstrating the feasibility of the separation approach in a complex biofluid. First results of a THP1 reporter assay showed increased Interferon pathway activation in RA synovial fluid-derived EVs.

Summary/Conclusion: Using a magnetic immunocapture approach, we were able to separate a CD90+ population from a heterogeneous mixture of in vitro fibroblast-derived EVs and also from synovial fluid spiked with CD90+ EVs. The ability to investigate distinct EV subsets present in biofluids of patients with various diseases may offer novel insights into their role in pathogenesis..

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