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OP 1
Incidence of COVID-19 in patients treated with infliximab compared to patients treated with rituximab
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Background: The prevalence of anti-SARS-CoV-2 IgG antibodies in the Geneva population was estimated at 9.7% end of April 2020. Immunosuppressed patients may be at increased risk of developing severe forms of COVID-19. It is unknown whether the increasing risk is due to immune-mediated diseases by themselves or to specific immunosuppressive therapies. We postulated that long-lasting cell-depleting therapies may increase the risk of severe COVID-19 more than targeted anti-cytokine therapies.

Objectives: To determine whether patients treated with rituximab (RTX) have more severe forms of COVID-19 compared to patients treated with anti-cytokine therapies, such as infliximab (IFX).

Methods: We included all patients who received infliximab or rituximab at the Rheumatology Division of the Geneva University Hospitals between January 1 and February 28, 2020. We called each patient and administered a questionnaire with predefined questions on COVID-19 symptoms and COVID-19 diagnosis occurring between 01.03.2020 and the 15.05.2020, which represents the first wave of the COVID-19 pandemic in Switzerland. We compared baseline characteristics using descriptive statistics.

Results: During the study period, 86 patients received either rituximab (RTX, n = 31) or infliximab (IFX, n = 55). We were able to retrieve complete COVID-19 information from 77 (90%) patients. Baseline characteristics in the two groups were balanced, but for significant differences in demographics in Switzerland. We compared baseline characteristics using descriptive statistics.

Conclusion: The incidence and prevalence of COVID-19 was similar in the two groups with axial spondyloarthritis is associated with improved retention of TNF inhibitors: results from the EuroSpA collaboration.


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OP 2
Co-medication with a conventional synthetic DMARD in patients with axial spondyloarthritis is associated with improved retention of TNF inhibitors: results from the EuroSpA collaboration.


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OP 3
Markers of extracellular markers turnover are altered in patients with very early systemic sclerosis
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Introduction: The very early diagnosis of patients with systemic sclerosis (veSSc) is important for a personalized follow-up and optimal timing of treatment. In this study, we hypothesise that changes in extracellular matrix (ECM) turnover, measured by ECM-degradation and formation markers are present very early in SSc, before clinical fibrosis occurs. We investigated serum-based ECM turnover markers as potential diagnostic biomarkers for veSSc.

Material and methods: Patients with veSSc, defined as presence of Raynaud’s syndrome and at least one of the following: puffy fingers, positive antinuclear antibodies or pathological nailfold capillaroscopy, without meeting any classification criteria for SSc, were included, and compared to healthy controls (HC, n = 29). Data and sera collection were conducted by EUSTAR/VEDOSS standards. ECM-degradation (BGM, C3M, C4M, C6M) and -formation markers (PRO-C3, PRO-C4, PRO-C5) were measured in serum using ELISA-based assays. The statistical analyses included Mann-Whitney U, Spearman correlation and ROC analysis.

Results: Compared to HC, veSSc patients had higher levels of degradation markers of type III and IV collagens (C3M, C4M, both p <0.0001) and of formation marker of type III collagen (PRO-C3, p = 0.0001) with an overall lower turnover of type III and IV collagen (PRO-C3/C4M, both p <0.0001). Higher levels of the biglycan degradation marker BGM (p = 0.005) and lower levels of the type VI collagen degradation marker C6M (p = 0.004) were observed in veSSc. In ROC analysis, markers of type III and IV collagen turnover could distinguish between veSSc and HC: C3M, AUC = 0.95, p <0.0001; C4M, AUC = 0.97, p <0.0001; PRO-C3/C4M, AUC = 0.80, p <0.0001; PRO-C4/C4M, AUC = 0.86, p <0.0001.

Conclusion: ECM turnover is altered in veSSc patients compared to HC. Biomarkers of type III and IV collagens could distinguish between veSSc patients and HC, which may indicate that these markers are potential diagnostic biomarkers complement clinical and immunological veSSc criteria to assess risk of developing fibrosis related to SSc.
A Case Of Not Anymore "Cryptogenic" Organizing Pneumonia.
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Background: Organizing pneumonia (OP) is a rare inflammatory and fibroproliferative process affecting the lungs with a clinicoradiological picture associating constitutional and pulmonary symptoms with alveolar opacities. Recovery is usually fast, complete and without sequelae, either naturally or after corticosteroid treatment. The majority of cases are cryptogenic (COP), but secondary organizing pneumonia (SOP) can occur, mainly related to drugs, infections and autoimmune diseases, in particular rheumatoid arthritis and myositis.

Case presentation: A 39-year-old Moroccan female patient presented in April 2019 in another hospital with an episode of cough, fever and basithoracic pain associated with systemic inflammation, radiographic left lung infiltrate and pleural effusion. All microbiological studies remained sterile and response to various antibiotics was poor. CT scan demonstrated a massive infiltrate of the left lower lobe and the final diagnosis of COP was made based on the bronchoalveolar lavage and the good response to corticosteroids, in the absence of obvious etiology. In October 2019, just after corticosteroids' discontinuation, the patient developed inflammatory axial pain and peripheral polyarthralgia, fatigue and night sweating. She also mentioned cutaneous photosensibility and familial history of Crohn’s disease. Acute phase reactants were again elevated, and MRI of the spine and sacroiliac joints demonstrated multiple erosions and signs of bilateral sacroilitis. HLA-B27 was negative.

She then developed successively oligoarthritis, fever, diarrhea and abdominal pain, as well as conjunctivitis, that retrospectively were recurrent for many years. She also presented new oral aphthous ulcers, enthesitis and signs of bilateral sacroilitis. HLA-B27 was negative. She then developed successively oligoarthritis, fever, diarrhea and abdominal pain, as well as conjunctivitis, that retrospectively were recurrent for many years. She also presented new oral aphthous ulcers, genital lesions, and a pathergy phenomenon. HLA-B51 was negative and the chest radiograph was now unremarkable. Fecal calprotectin were recurrent for many years. She also presented new oral aphthous ulcers, genital lesions, and a pathergy phenomenon. HLA-B51 was negative and the chest radiograph was now unremarkable. Fecal calprotectin were high, and MRI of the spine and sacroiliac joints demonstrated multiple erosions and signs of bilateral sacroilitis. HLA-B27 was negative.

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Conclusion: This case demonstrates a rare association of OP with Behçet’s disease. It also shows that even if OP is often cryptogenic and its course usually rapidly favorable, it can also be the initial mode of presentation of an autoimmune disease.

Idiopathic Granulomatous Mastitis Successfully Treated With Leflunomide: A Case Report.
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Background: Idiopathic granulomatous mastitis (IGM) is a rare, benign, chronic inflammatory breast disease of unknown origin. It mimics abscess or breast cancer, and primarily affects young and childbearing women, often with a history of breastfeeding and originating from Middle East, Hispanic, Mediterranean and Asian countries. Due to the rarity of the condition, diagnosis and treatment remain a challenge.

Case presentation: A 35-year-old female Afghan patient, with a pertinent medical history of three pregnancies (all breastfed) and one lactation unrelated mastitis, presented with multiple inflammatory painful masses of her right breast, complicated by two ulcerations and fistulae with serosanguineous discharge and an axillary adenopathy. Except for chronic fatigue, the rest of history and examination was not contributive. Several courses of empiric and systemic antibiotics were ineffective. Cultures of the discharge fluid was sterile. A first biopsy mentioned an abscessed cystic lesion. A second study demonstrated multiple enhancing lesions and an axillary adenopathy. New biopsies highlighted fibro-inflammatory changes with non-caseating granuloma and giant cells, and a reactive lymph node. All microbiological analyses performed (cultures, Gram, Ziel-Hielsel, PAS and Grocott stains, mycobacterial PCR) were negative. Blood tests showed no systemic inflammation, normal ACE and lysozyme, negative IGRA, ANCA and ANA tests. Chest radiograph was normal. Despite high-dose corticosteroids for an IGM diagnosis, alone and in combination with methotrexate and hydroxychloroquine, disease control was unsatisfactory. However, switch to leflunomide greatly improved disease control with an almost total recovery and remission to date.

Conclusion: IGM is an uncommon inflammatory disease with mostly a protracted course and a high impact on quality of life in a generally young patient population. This condition remains a challenge both in terms of diagnosis and treatment. If high dose corticosteroids and methotrexate are common recommended treatment options with surgery, our case demonstrated significant response to leflunomide. This could be an interesting option when corticosteroids with or without methotrexate failed, allowing avoidance of surgery with unaesthetic and uncertain results.
knees were swollen, with marked, painful, limitation of right hip and left shoulder range. Synovial fluid of the knee and hip was inflammatory (14000 leuc/mm3), with no crystal neither bacteria, mycobacteria nor fungus. Blood inflammatory markers were moderately elevated (CRP 21mg/L, ESR 44). X-rays confirmed destructive arthropathy. Due to African origin and rapid joint destruction, we first looked for an infectious disease, however serology for hepatitis, HIV, HTLV-1, Leishmania, Brucella, Bartonella and Lyme disease were negative. A negative Quantiferon-TB gold test as well as a normal chest x-ray were against tuberculosis or sarcoidosis. Hands and feet X-ray did not show erosion. The immunological assessment was negative for rheumatoid factor, anti-CCP and AAN. A thoraco-abdomino-pelvic CT scan was not relevant.

Finally, in front of an unclassifiable oligoarthritis, we did a Tropheryma whippelii-PCR in saliva and stool, which turn out to be positive. A duodenal biopsy confirmed the diagnosis of WD. There was no neurological, cardiac or ophthalmological involvement on extensive assessment. Patient was put on treatment with hydroxychloroquine and doxycline according to the recommendations.

Joint symptoms are common in WD, reported in up to 80 percent of patients, among migrants described an intestinal colonization in 11.2% of African and 10.8% of Latin American. It is therefore important to think about WD also in a migrant’s population in front of an unclassified arthritis.

C 5
Symptomatic heterozygous Familial Mediterranean Fever successfully treated with canakinumab: a case report
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We present the case of a 35-year-old Portuguese patient presenting initially in 2010 spontaneously resolving episodes of high fever for several weeks. Afterward, she suffered self-limited attacks lasting a few days of polyarthralgia without synovitis, or unrelated attacks of cutaneous lesions lasting a few hours, all without any fever. She also complained of multiple unspecific symptoms with recurrent headaches, permanent fatigue, intermittent abdominal pain and diarrhea, exertional dyspnea and oral ulcers, without any history of genital ulcers or uveitis.

In 2019, she presented again recurrent episodes of fever lasting 1 to 3 days, often peaking in the evening. There were no clinical, biological or radiological arguments for infection, neoplasia or autoimmune disorder, but a heterozygous mutation of a Met694Val for the MEFV gene.

FMF is associated with mutations in the MEFV gene, which encodes the inflammasome adaptor pyrin, and is classically defined as an autosomal recessive disease characterized by recurring short episodes of fever, polyserositis and arthritis. Nevertheless, as this case illustrates, heterozygous mutation carriers can suffer from a mild or incomplete form of FMF which can mimic many rheumatologic diseases with atypical symptoms. Up to 40% of patients with a clinical diagnosis of FMF carry a single or no MEFV mutation, and another study found that, in 20–25% of patients, only one MEFV gene mutation can be detected despite complete sequencing of the gene. It is now clear that FMF can be caused by a single MEFV mutation, with the influence of other modifiers genes or environmental factors contributing to the variable penetrance and the phenotypic variability.

In a retrospective study, both M694V homozygosity and heterozygosity were associated with increased risk of AA amyloidosis, and M694V mutation is considered an important predicting factor of this complication. In this context, we treated our patient and, while colchicine was partially effective, she demonstrated excellent response to canakinumab, confirmed by recurrence of attacks when treatment was temporarily discontinued.

In conclusion, this case demonstrates that FMF should be part of a wider differential diagnosis, even in the presence of atypical symptoms, and that heterozygosity does not prevent phenotypic disease. Interestingly, the same mutation was found in the patient’s mother, son, aunt and nephew, which all have similar symptoms.

C 6
An unusual case of leptomeningitis
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We report the case of a 79-year-old woman hospitalized to investigate a 12 kg weight loss over the last 3 months with intermittent joint pain (ankles), dry eyes, dry mouth, chronic headaches and dizziness. The clinical examination revealed a patient with a decreased general condition, reduced salivary pool, with no lymphadenopathy, synovitis or skin abnormality. The neurological status was normal.

The investigations showed elevated ESR (62 mm/h), high ANA titer (1:2560), positive anti-ENA with specificity for anti-SSA and anti-gp210. Anti-dsDNA were negative but anti-CCP were positive (146U). There was no complement consumption, no monoclonal gammapathy and no cryoglobulinemia. Urine analysis showed no proteinuria or hematuria. A PET-CT revealed mediastinal and hepatic lymphadenopathies. There was no evidence of neoplasia on PET-CT, immunoelectrophoresis and gynecological examination. An infectious cause was ruled out, especially Lyme disease, syphilis, viral hepatitis and Whipple disease. Schirmer’s test and sialometry were both pathological. Minor salivary glands biopsy confirmed a focal lymphocytic sialadenitis (focus score >1). Cerebral MRI showed a focal leptomeningitis without encephalitis. Cerebrospinal fluid analysis identified increased protein levels consistent with a sterile lymphocytic meningitis.

We retained the diagnosis of Sjögren’s syndrome, according to ACR-EULAR2016 criteria, with central nervous system (CNS) impairment, sicca and constitutional symptoms (ESSDAI 25). We did not observe any articular activity related to anti-CCP antibodies.

This clinical presentation of Sjögren’s syndrome is rare. The overall prevalence of neurologic disease in pSS is approximately 20% and CNS involvement affects only 1-5% of the patients. Anti-gp210 are usually associated with primary biliary cholangitis, which can occur along with Sjögren’s syndrome, but in this patient, there was no cholestasis.

Due to concerns about treatment tolerance in this frail patient, we choose to treat her with rituximab and systemic glucocorticoids instead of cyclophosphamide. The treatment was well tolerated and the patient showed a good response after a follow-up of 6 months. Constitutional symptoms resolved. The patient regained weight and energy. Brain MRI showed an improvement of focal leptomeningitis.

In conclusion, we report a case of Sjögren’s syndrome with severe CNS involvement successfully treated with rituximab after 6 months of follow-up.
Efficacy and safety of tocilizumab in patients with giant cell arteritis and visual impairment
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Background: Tocilizumab (TCZ) represents a potent new therapeutic principle for patients with GCA, however, data on efficacy and safety in patients who present with visual affection is still limited.

Objective: To study the outcome of patients with GCA and visual affection treated with TCZ.

Methods: This retrospective analysis was performed on all patients with GCA and visual disturbances consecutively recruited between April 2013 and May 2020 who underwent treatment with tocilizumab in addition to corticosteroids.

Results: 19 GCA patients (14 women, 5 male) with a mean age of 73.4 + 10 yrs at GCA diagnosis and 28 affected eyes were treated with tocilizumab in addition to corticosteroids. 4/19 patients presented with visual disturbances on oral prednisone and 2/19 patients were on csDMARDs (leflunomide, MTX) for polymyalgia. 2 patients experienced unilateral blindness while receiving iv pulse corticosteroids. AAION was diagnosed in 23/28 eyes, PION in 1/28 eyes and occlusion of the central retinal artery in 4/28 eyes. Loss of vision below 0.1 BCVA occurred in 12/28 eyes. Non patients had bilateral blindness at baseline. 5/28 eyes were affected by sectoral anopia, impaired vision was reported in 11/28 eyes. 17 patients were treated with TCZ iv 8mg/kg every 4 weeks, 2 patients received TCZ sc at 162mg every 2 weeks. All patients with visual symptoms received intravenous steroid boluses, followed by prednisone 1mg/kg/day with subsequent tapering. Mean disease duration before initiation of tocilizumab was 1.8 + 1.7 months. 11/19 patients started with TCZ within 6 weeks after diagnosis of GCA, in 3 patients TCZ was started because of refractory and/or relapsed disease. Mean duration of TCZ therapy was 18.9 + 11.5 months. 14/19 patients were able to stop steroids (GC) after a mean duration of 16.7 + 14.8 months and have been steroid-free for an average time of 15 + 10.4 months. In addition to cessation of GC, 8 patients have discon-tinued TCZ, 2 patients relapsed after 11 and 14 months. At present, 6 patients remain drug-free for 3 to 28 months (16 + 11 months). None of the 12 eyes with vision < 0.1 BCVA recovered, but no new vision disturbances occurred during TCZ or after cessation of either TCZ or GC.

Conclusions: Inhibition of IL-6 with TCZ represents a safe treatment option to prevent deterioration of visual complications in GCA patients with initial visual impairment.

P 3

Efficacy of adjunctive methotrexate in patients with Giant Cell Arteritis treated with tocilizumab plus prednisone tapering: subanalysis of the GIACTA trial
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Background: Evidence regarding the efficacy of methotrexate (MTX) in patients with giant cell arteritis (GCA) conflicts, and the benefit of adjunctive MTX treatment is unclear. Here, we present data from a subanalysis of the 52-week, double-blind, randomized controlled GIACTA trial in a subgroup of patients with GCA who received MTX in addition to tocilizumab (TCZ) or placebo (PBO) in combination with prednisone tapering.

Objectives: Assess the efficacy of adjunctive MTX in patients with GCA.

Methods: In part 1 of GIACTA, patients were randomly assigned to TCZ administered subcutaneously every week or every other week plus 26-week prednisone tapering or PBO plus 26-week or 52-week prednisone tapering for achieving sustained glucocorticoid-free remission in patients with giant cell arteritis (GCA). Among patients with new-onset GCA at baseline, both TCZ regimens reduced the risk for GCA flare compared with PBO+26. Among patients with relapsing GCA, only TCZ QW treatment reduced the risk for flare compared with both PBO groups. Here, we report time to first flare over 3 years of the GIACTA trial (1-year part 1 + 2-year open-label part 2) among patients with new-onset or relapsing GCA.

Methods: After part 1, patients entered open-label part 2, where the investigator decided GCA therapy (including initiation/termination of open-label TCZ and/or glucocorticoids) according to disease status. Time to first flare during the entire trial was assessed using Kaplan-Meier analysis (intent-to-treat population) according to disease status at baseline (new-onset or relapsing) based on initial treatment groups: TCZ QW, TCZ Q2W, or pooled PBO.

Results: Among patients randomly assigned in part 1, approximately half of each group had new-onset GCA (Table). Median time to first flare over 3 years was longer for patients assigned to TCZ treatment in part 1 than for those assigned to PBO for both disease onset subgroups. Lower proportions of patients in the TCZ QW group experienced a flare during the entire study (51% new-onset; 53% relapsing) than the pooled PBO group (72% new-onset; 69% relapsing) and the TCZ Q2W group (73% new-onset; 65% relapsing). Kaplan-Meier analysis of time to first flare showed a clear separation between the TCZ QW and pooled PBO groups over 3 years for both disease onset subgroups. Separation of curves between the TCQ QW and TCQ Q2W groups was also observed for both disease onset subgroups, although more accentuated in patients with new-onset GCA.

Conclusion: In this 3-year analysis of GIACTA, time to first flare favored TCZ QW over TCZ Q2W in patients with new-onset and relapsing GCA. TCZ QW delayed time to first flare compared with PBO in patients regardless of disease onset, supporting TCZ QW dosing in patients with GCA.

Reference
TCZ (MTX 0.76 vs no MTX 0.47; p = 0.2549) or PBO (MTX 1.89 vs no MTX 1.46; p = 0.4611) groups. Rates of adverse events per 100 patient-years were numerically higher in MTX-treated patients (TCZ+MTX 1267, TCZ 858; PBO+MTX 1331, PBO 952).

Conclusion: Preliminary data from a small subgroup of patients suggest that adjunctive MTX does not increase the likelihood of sustained remission, reduce relapse rate, or improve steroid sparing in patients with CCP. Response rates in TCZ-treated patients appear to be independent of treatment with MTX. These results should be confirmed in larger studies.

Reference

P 4

Serum calprotectin: a promising biomarker in rheumatoid arthritis and axial spondyloarthritis
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Background: Calprotectin (S100A8/S100A9 protein) is known as a damage-associated molecular pattern (DAMP) protein and reflects mainly neutrophil activation. Serum calprotectin levels may serve as an alternative to acute-phase proteins as a biomarker in inflammatory rheumatic diseases. The aim of this study is to investigate the association of serum calprotectin with disease activity and severity in rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).

Methods: Serum calprotectin was measured in patients with RA, axSpA and PsA from the prospective Swiss Clinical : Quality Management (SCQM) registry. Asymptomatic first-degree relatives of RA patients were used as healthy controls (HC). Outcomes included swollen joint count (SJC), Disease Activity Score (DAS), Health Assessment questionnaire (HAQ), joint radiographs and ultrasound power Doppler (USPD) score for RA; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS) and coxitis for axSpA; SJC, Disease Activity Index for Psoriatic Arthritis (DAPSA) for PsA. Comparison of outcomes by calprotectin quartile levels was performed using Kruskal-Wallis tests for continuous outcomes and chi-square tests for categorical outcomes.

Results: A total of 1729 subjects [RA = 969, axSpA = 451, PsA = 237 and HC = 72] were included. Median levels of serum calprotectin were higher in each disease group compared to HC (p < 0.01). In RA patients, all clinical outcomes were statistically different between quartiles of serum calprotectin, indicating an association between calprotectin levels and higher disease activity (SJC, DAS and USPD scores) and severity (joint radiographs and HAQ). This association remains true for SJC in a subgroup of RA patients with high reactive protein (CRP) elevation. Calprotectin seemed more accurate than CRP to discriminate disease activity in a subgroup of RA treated with tocilizumab. In axSpA, an association between calprotectin levels and ASDAS score (<0.01) and prevalence of hip involvement (p = 0.02) was observed. For PsA patients, SJC and DAPSA did not differ across calprotectin quartiles.

Conclusions: This large study supports the association of serum calprotectin levels with disease activity in both RA and axSpA, but not in PsA. Serum calprotectin may constitute a useful biomarker when determination of acute-phase proteins cannot be reliably used such as in patients on anti-IL-6 therapies.

P 5

The Impact of Persistent Inflammatory Changes on Prevalence of Fat Lesions in Patients with Axial Spondyloarthritis Treated with Certolizumab Pegol: 4-Year MRI Results from RAPID-axSpA
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Background: Fat lesions (FLs) on magnetic resonance imaging (MRI) T1 sequences are considered to be precursors of structural damage in axial spondyloarthropathies (axSpA) patients. Certolizumab pegol (CZP), an Fc-free, PEGylated tumour necrosis factor inhibitor has been shown to decrease spinal and sacroiliac joint MRI inflammation and limit spinal radiographic progression over 4 years of treatment. We report the effect of early post-baseline (BL) inflammatory changes on FL prevalence over 4 years in CZP-treated axSpA patients from RAPID-axSpA (NCT01087762).

Methods: RAPID-axSpA was a phase 3 trial, double-blind and placebo (PBO)? controlled to Week (Wk) 24, dose?blinded to Wk48 and open-label to Wk204. CZP randomised patients (Wk0 CZP: 200 mg every 2 wks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO? randomised patients received CZP from Wk24, or from Wk16 if non-responders. Blinded spinal MRI scans were evaluated for FLs and inflammatory lesions in vertebral edges (VEs) at Wk0/12/48/68/204. FL prevalences are reported as odds ratios (estimated from a logistic regression model [OR; FL+/FL-]) between time points/inflammation states, with nominal 95% confidence intervals (CI).

Results: Of 325 axSpA patients, 89 and 47 initially randomised to CZP or PBO, respectively, were eligible (had a BL and ≥1 post-BL MRI). 2,047 VEs were assessed at BL: inflammation was observed in 21.2% (mean count: 5.0/patient), FL in 29.8% (mean count: 6.8/patient) and both in 10.6% of VEs. At BL, FLs were more often observed in inflamed VEs vs non-inflamed VEs (OR: 3.06; 95% CI: 2.14, 4.35). This difference increased over time: FLs were more frequently observed at Wk204 vs BL in VEs that were inflamed at BL (4.91; 2.58, 9.32) compared with VEs that were not inflamed at BL (1.15; 0.78, 1.72). Resolution of inflammation by Wk12 appeared to lower the risk of FL prevalence over 4 years. When adjusted for BL VE status, FLs were more often observed in VEs with vs without Wk12 inflammation at Wk12 (1.49; 0.41, 5.36), Wk96 (2.91; 0.82, 10.40) and Wk204 (6.35; 1.56, 24.32).

Conclusion: Inflammation that prevailed after CZP treatment initiation was associated with increased FL prevalence over 4 years. Reduction of inflammation by Wk12 reduced the risk of FL long-term, indicating the importance of early treatment initiation in axSpA patients.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical.

P 6

52-Week Efficacy and Safety of Ixekizumab in Radiographic Axial Spondyloarthritis/Aankylosing Spondylitis Patients naïve to biologic treatments or with prior Inadequate Response/Intolerance to Tumor Necrosis Factor Inhibitors
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Background: Radiographic axial spondylitis (r-axSpA), or Ankylosing Spondylitis (AS), is a chronic inflammatory disease of the axial skeleton associated with serious pain, stiffness and limited flexibility, impairing quality of life. Two clinical trials demonstrated efficacy and safety of ixekizumab (IXE), a humanised anti-IL-17 IgG4 antibody, in r-axSpA/PS patients naïve to biologics, or with prior inadequate response/intolerance to Tumor Necrosis Factor inhibitors (TNFI) over 16 weeks. This study assessed the treatment effect over 52 weeks. Additionally, the influence of baseline inflammation, measured by C-reactive protein (CRP) and/or spinal MRI on ASAS40 response at week 16 was investigated.

Methods: Data from two Phase 3, randomized, double-blind, placebo (PBO)-controlled trials, with patients who fulfilled the Assessment of SpondyloArthritis International Society (ASAS) criteria for AS and were either biologic-naïve (COAST-W, NCT02696798) or TNFi-experienced (COAST-W, NCT03269785), were analysed. We compared the proportion of patients achieving ASAS20/40, a 50% improvement of baseline Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and assessed the change in spinal pain. Missing data was handled by using non-responder imputation for ASAS20/40 and BASDAI response rates and ASAS40. Baseline Observation Carried Forward (BOCF) was used for spinal pain change from baseline. To investigate the influence of baseline inflammation on the efficacy, we examined the ASAS40 response at week 16 by baseline CRP (normal; ≤5 or elevated; >5 mg/L) and/or MRI Spondyloarthritis Research Consortium of Canada (SPARCC) spine score (<2 or ≥2) using an integrated COAST-W/VA dataset.

Results: At week 16, significantly more IXE than PBO-treated patients achieved ASAS20/40 and BASDAI50 and a decrease in spinal pain. Decreases in disease activity were maintained through week 52. These outcomes occurred in both biologic-naïve and TNFI-experienced patients. Safety outcomes were consistent with previous IXE studies. At week 16,
in the integrated dataset, significantly more IXE than PBO-treated patients achieved ASAS40 response regardless of baseline CRP or MRI spine SPARCC score.

Conclusion: Through week 52, treatment with IXE resulted in sustained efficacy in biologic-naïve and TNF-α-experienced AS patients with no unexpected safety signals. Furthermore, at week 16, IXE demonstrated efficacy (ASAS40) irrespective of baseline CRP levels or spinal MRI score.

P 7

Comparative effects of ixekizumab vs adalimumab across psoriatic arthritis patients defined by baseline characteristics: week 24 outcomes from SPIRIT-H2H

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Background: Ixekizumab (IXE), an IL-17A antagonist, showed superiority over TNF-inhibitor adalimumab (ADA) for the simultaneous achievement of ACR50 and PASI100, and PASI100 alone in the SPIRIT-H2H trial at week 24. We analysed differences in efficacy outcomes between IXE and ADA by subgroups.

Methods: We conducted post-hoc analysis of data from SPIRIT-H2H (NCT03151551), a 52-week, multicentre, open-label, blinded assessor study with active PsA (defined as swollen joint count ≥3 and tender joint count ≥3), with a body surface area [BSA] ≥3% and inadequate response to conventional synthetic (cs)-DMARDs and naive to biologic (b)-DMARDs. Patients were randomised 1:1 to IXE or ADA, while presence/absence of moderate-to-severe psoriasis (defined as PASI ≥12, static Physician Global Assessment ≥3 and BSA ≥10%) determined on-label dosing. Subgroups were defined by baseline enthesitis, dactylitis, fingernail psoriasis (presence/absence), BSA (<10%, >10%), and CRP (≥10%)

Fisher’s exact test was used for between group comparisons of efficacy outcome measures at 24-weeks (PASI90, ACR50, and minimal disease activity [MDA]). Missing data were overcome by non-responder imputation. Nine pts with active PsO and BSA≥3% were assessed as PASI = 0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI = 0 and BSA = 0 at post baseline visits.

Results: At week24 IXE and ADA demonstrated comparable efficacy in ACR50 response rates across all subgroups. ACR70 response in patients with fingernail psoriasis was significantly greater with IXE-treated vs ADA (p = 0.02). PASI90 response with baseline enthesitis (p <0.001), with dactylitis (p <0.001), with fingernail psoriasis (p <0.001), CRP (≥6mg/L, ≥6mg/L) (p = 0.003; ≥6mg/L, ≥6mg/L) (p = 0.036) and BSA ( <10%, p = 0.010; ≥10%, p = 0.003) was significantly greater in IXE vs ADA. Significantly more IXE-treated patients vs ADA achieved MDA with baseline enthesitis (p = 0.002), without dactylitis (p = 0.015), with fingernail psoriasis (p <0.001), CRP (≥6mg/L, p = 0.046) and BSA ≥10% (p = 0.01). A limitation is that this analysis was completed post-hoc, not controlled for multiplicity, and patients were not stratified by baseline disease characteristics.

Conclusions: IXE and ADA are associated with comparable efficacy and associated with a greater effect in certain subgroups. Results will aid clinicians when making treatment choices.

P 8

Ixekizumab vs. adalimumab for the treatment of psoriatic arthritis: 52-week efficacy and safety outcomes

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Background: At week 24 of the SPIRIT H2H study in patients with active psoriatic arthritis (PSA), ixekizumab (IXE) showed superiority to adalimumab (ADA) for the simultaneous achievement of ACR50 and PASI100. Here we report the 52-week efficacy outcomes including individual ACR components and in subgroups +/- concomitant methotrexate (MTX).

Methods: SPIRIT H2H (NCT03151551) was a 52-week, multicentre, open-label, blinded-assessor study of bDMARD naïve patients with active PSA (defined as swollen joint count ≥3/68, and tender joint count ≥3/66), with a body surface area [BSA] ≥3% and inadequate response to conventional synthetic (cs)-DMARDs. Patients were randomised 1:1 to IXE or ADA, stratified by baseline enthesitis and dactylitis, with presence of moderate-to-severe psoriasis (defined as Psoriasis Area and Severity Index [PASI] ≥12 combined with a static Physician Global Assessment ≥3 and BSA ≥10%). Patients received approved label dosing of assigned treatment dependent on presence/absence of moderate-to-severe psoriasis. Primary outcome was achievement of simultaneous ACR50 + PASI100; secondary outcomes were achievement of PASI100, ACR20/50/70 and changes in individual ACR component scores. Nine pts with active PsO and BSA≥3% were assessed as PASI = 0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PAS100 responders if PASI = 0 and BSA = 0 at post baseline visits. Data were analysed using logistic regression with non-responder imputation for missing data.

Results: Baseline characteristics were balanced across treatment groups. At week 52, a significantly larger percentage of IXE- vs. ADA-treated patients achieved simultaneous ACR50 + PAS100 and ACR100, consistent with 24-week results. IXE performed at least as well as ADA at week 52 for all other outcomes. With/without MTX, IXE efficacy was consistent at week 52 across ACR20/50/70 with a significantly greater achievement of simultaneous ACR50+PASI100 and ACR70. IXE- versus ADA-treatment resulted in comparable changes from baseline for each individual ACR component at week 52. Safety was consistent with previous reports.

Conclusions: In patients with PSA, treatment with IXE versus ADA resulted in a significantly greater achievement of simultaneous skin and joint improvement at week 52, consistent with week 24 results. At week 52 consistent efficacy was shown for IXE when used with/without MTX.

P 9

Efficacy and Safety of 108 Weeks of Bimekizumab Treatment in Patients with Psoriatic Arthritis: Interim Results from a Phase 2 Open-Label Extension Study

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Background: Bimekizumab (BZK), a monoclonal antibody which selectively neutralises IL-17A and IL-17F, has shown clinical improvements in joint and skin outcomes over 48 weeks (wks) in patients (pts) with active psoriatic arthritis (psA). A two-year interim results are reported from the phase 2b, dose-ranging study of BZK in pts with psA and inadequate response to TNF-inhibitor adalimumab (ADA) at week 108 (NCT02969525) and ongoing open-label extension (OLE): BE ACTIVE 2; NCT03347110.

Methods: Study design has been described elsewhere.1 Pts who completed 48 wks’ BZK treatment without meeting withdrawal criteria were eligible for OLE entry. All OLE pts received BZK 160 mg Q4W, irrespective of prior dosing regimen. Data are presented from BE ACTIVE baseline (BL) to OLE Wk60 (Wk108 total). Efficacy outcomes are reported for the full analysis set: pts who received ≥1 dose BZK (specifically those randomised to 160mg, 160mg with 320mg loading dose [LD] or 320mg at BL), with BL efficacy measurements to allow subsequent determination of ACR50. Outcomes include ACR20/50/70, body surface area (BSA) %, minimal disease activity (MDA), and enthesitis/dactylitis resolution. Rates of treatment-emergent adverse events (TEAEs) are reported for the safety set (SS; pts who received ≥1 dose BZK in the dosing ranging study). Non-responder imputation rates for outcomes are reported unless stated otherwise.

Results: Of 123 pts randomised to BZK 160/160(LD)/320mg, BL mean (SD) tender/swollen joint counts were 21.7: (15.7)/11.2 (8.4). 80 (65.0%) pts had BSA≥3% and inadequate response to ADA at week 52 for all other outcomes. With/without MTX, BZK efficacy was consistent at week 52 across ACR20/50/70 with a significantly greater achievement of simultaneous ACR50 + PASI100 and ACR70. BZK versus ADA-treatment resulted in comparable changes from baseline for each individual ACR component at week 52. Safety was consistent with previous reports.

Conclusions: BZK treatment resulted in a significantly greater improvement of simultaneous skin and joint outcome improvement at week 52, consistent with week 24 results. At week 52, consistent efficacy was shown for BZK when used with/without MTX.
Background: In many countries, JAK-inhibitors (JAKi) have only recently been approved as treatment for patients with rheumatoid arthritis (RA).

Objective: To evaluate the effectiveness of JAKi compared to bDMARDs in RA patients in the real-world population in an international collaboration of registers (the “JAK-pot” collaboration).

Methods: Patients initiating either JAKi, TNFi, IL-6i or abatacept (ABA) during a time period when JAKi were available in each country (19 registers, Table) were included. We compared the effectiveness of JAKi and bDMARDs in terms of retention using crude and adjusted survival analysis. Missing covariates were imputed using multiple imputation.

Results: Among 25521 included patients, 6063 initiated a JAKi, 13879 a TNFi, 2348 ABA, and 3231 an IL-6i. Patients were on average 55 years old, with a mean disease duration 10 years, mostly seropositive (67%), female (77%) and with moderate disease activity at treatment initiation. The main reason of stopping treatment was ineffectiveness (49%), followed by adverse events (21%). Patients on JAKi were treated more often as monotherapy, had higher CRP and disease activity at baseline and had experienced more previous ts/bDMARDs. Crude median retention was 1.4 (95% CI 1.2-1.5) years for JAKi, 1.6 (1.6-1.7) for TNFi, 1.5 (1.3-1.7) for IL6i and 1.1 (1.0-1.3) for ABA. After adjustment, the hazard ratio (HR) for discontinuation tended to be lower for JAKi (HR 0.86 (0.65-1.13)) compared to TNFi, but comparable for ABA (1.02 (0.94-1.10)) and IL6i (0.99 (0.88-1.10)). HRs differed notably between countries.

Conclusion: The adjusted overall drug retention of JAKi tended to be higher than for TNFi, with large variation between countries. Other measures of effectiveness, such as the evaluation of CDAI remission and low disease activity are planned to shape a more comprehensive picture of JAKi effectiveness in the real world.

P 12

Human Synovium at Single-Cell Resolution

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Single-cell RNA sequencing (scRNA-seq) technologies have revolutionized our understanding of cell complexity and tissue dynamics in the human body. Here we constructed a comprehensive landscape of the cell types and molecular pathways in human synovium by integrating our newly generated synovial scRNA-seq data with published synovial scRNA-seq studies. The scRNA-seq datasets were generated across three scRNA-seq technologies using dissociated sorted and unsorted cells. ScRNA-seq data were analyzed using Seurat. We identified synovial cell clusters and their marker genes, followed by functional gene enrichment analysis. Additionally, we mapped the canonical cell markers, such as CD3 and CD79 canonical T and B cell markers, to the clusters. The meta-analysis of our and published scRNA-seq studies included 33 donors yielding 42000 high-quality scRNA-seq cell profiles. We identified five different subtypes of synovial fibroblasts, including lining and sublining fibroblasts, three subtypes of synovial monocytes/macrophages, two distinct B cell subsets, several T cell subsets, NK cells as well as endothelial cells. Through integrated analysis, we were able to detect a small population of previously undescribed fibroblast-like cells in human synovium. These cells were located around the fibroblast clusters and represented a mixed population of CD54-, podoplanin (PDPN)high and PDPNlow cells, mostly negative for the sub-lining fibroblast marker THY. They were enriched in cell division/cell cycle genes and expressed many extracellular matrix genes which suggested their potential stromal progenitor status. The gene expression profile of these cells inclined towards cell migration, vascular development and insulin growth factor-dependent processes. Our data considerably increased the number of identified scRNA-seq cell profiles in the human synovium. We demonstrated the depth of synovial scRNA-seq dataset across different technologies and protocols and advanced the understanding of human synovial biology.

P 11

Comparative effectiveness of JAK-inhibitors, TNF-inhibitors, abatacept and IL-6 inhibitors in an international collaboration of registers of rheumatoid arthritis patients (the “JAK-pot” study)

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Single-cell RNA sequencing (scRNA-seq) technologies have revolutionized our understanding of cell complexity and tissue dynamics in the human body. Here we constructed a comprehensive landscape of the cell types and molecular pathways in human synovium by integrating our newly generated synovial scRNA-seq data with published synovial scRNA-seq studies. The scRNA-seq datasets were generated across three scRNA-seq technologies using dissociated sorted and unsorted cells. ScRNA-seq data were analyzed using Seurat. We identified synovial cell clusters and their marker genes, followed by functional gene enrichment analysis. Additionally, we mapped the canonical cell markers, such as CD3 and CD79 canonical T and B cell markers, to the clusters. The meta-analysis of our and published scRNA-seq studies included 33 donors yielding 42000 high-quality scRNA-seq cell profiles. We identified five different subtypes of synovial fibroblasts, including lining and sublining fibroblasts, three subtypes of synovial monocytes/macrophages, two distinct B cell subsets, several T cell subsets, NK cells as well as endothelial cells. Through integrated analysis, we were able to detect a small population of previously undescribed fibroblast-like cells in human synovium. These cells were located around the fibroblast clusters and represented a mixed population of CD54-, podoplanin (PDPN)high and PDPNlow cells, mostly negative for the sub-lining fibroblast marker THY. They were enriched in cell division/cell cycle genes and expressed many extracellular matrix genes which suggested their potential stromal progenitor status. The gene expression profile of these cells inclined towards cell migration, vascular development and insulin growth factor-dependent processes. Our data considerably increased the number of identified scRNA-seq cell profiles in the human synovium. We demonstrated the depth of synovial scRNA-seq dataset across different technologies and protocols and advanced the understanding of human synovial biology.

P 10

Personalized Prediction of Disease Activity in Patients with Rheumatoid Arthritis using an Adaptive Neural Network

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Background: Rheumatoid arthritis (RA) lacks reliable biomarkers that predict disease resolution on an individual basis, potentially leading to over- and undertreatment. Deep neural networks learn from former experiences on a large scale and can be used to predict future events as a potential tool for personalized clinical assistance.

Objective: To investigate deep learning for the prediction of individual disease activity in RA.

Methods: Demographic and disease characteristics from over 9500 patients and 65,000 visits from the Swiss Quality Management (SCQM) data bank were used to train and evaluate an adaptive network (AdaptiveNet). Patient and disease characteristics along with clinical and patient reported outcomes, laboratory values and medication were used as input features. DAS28-BSR was used to predict active disease and future numeric individual disease activity by classification and regression, respectively.

Results: AdaptiveNet predicted active disease defined as DAS28-BSR >2.6 at the next visit with an overall accuracy of 75.6% and a sensitivity and specificity of 84.2% and 61.5%, respectively. Apart from DAS28-BSR, the most influential characteristics to predict disease activity were joint pain, disease duration, age and medication. Longer disease duration, age >50 years or antibody positivity marginally improved prediction performance. Regression allowed forecasting individual DAS28-BSR values with a mean squared error of 0.9, corresponding to a variation between predicted and true values at next visit of 8%.

Conclusion: Deep neural networks have the capacity to predict individual disease outcome in RA. Low specificity remains challenging and might benefit from alternative input data or outcome targets.
Real world effectiveness of baricitinib in the Swiss rheumatoid arthritis register (SCQM-RA)

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Background: Patients with rheumatoid arthritis (RA) intolerant or not responding adequately to conventional synthetic DMARD (csDMARD) usually receive biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) as 2nd line. Baricitinib (BARI), a once-daily oral selective Janus kinase inhibitor, is efficient in randomised controlled trials but still lacks evidence for effectiveness in real world settings.

Objectives: To characterise patients initiating treatment with BARI or other alternative bDMARDs, and to perform an analysis of drug maintenance.

Methods: This is an observational, prospective, cohort study, within the Swiss Clinical Quality Management register. All treatment courses (TC) initiated between 2017-09-01 and 2019-10-01 were considered, comparing TC with BARI (BARI group) to TC with alternative bDMARDs, either TNF inhibitors (TNFi group) or other mode of action bDMARDs (OMA group), excluding rituximab. Baseline characteristics were compared using ANOVA or χ² tests. The crude drug maintenance was assessed by survival analysis (Kaplan-Meier). To correct for potential confounding factors, a Cox proportional hazard model was used. Missing values were imputed using multiple imputation with chain equations.

Results: During the study period, 979 TC were initiated (240 in BARI group, 461 in TNFi group and 278 in OMA group). BARI was prescribed to significantly older patients, with longer disease durations and more previous treatment failures. Unadjusted drug maintenance was significantly shorter in the TNFi compared to the BARI group (log rank p = 0.019). After adjustment for potential confounding factors, the hazard of TNFi discontinuation remained higher than for BARI (Hazard Ratio (HR) 1.48 (95% CI [1.05 – 2.09]; p = 0.02)). A similar trend was observed when comparing the OMA drugs to BARI, with a HR for discontinuation of 1.42 (95% CI [0.98 – 2.05]; p = 0.06). Covariates significantly associated with decreased drug maintenance were concomitant csDMARD and concomitant glucocorticoids.

Conclusions: In this preliminary analysis, baricitinib was prescribed to older patients, with longer disease durations, and more previous treatment failures compared to alternative bDMARDs. Baricitinib demonstrated a significantly higher drug maintenance than TNFi, while similar trend was observed in comparison to OMA drugs.

Conflict of interest: This analysis has been made possible by financial support of Eli Lilly (Swiss) SA to the Geneva University Hospitals.
patients. Additionally, W24 remission rates following treatments 1 or 3 were higher vs methotrexate monotherapy and numerically higher vs treatment 2.

Reference

P 16
Efficacy and Safety of Filgotinib in Methotrexate-Naive Patients with Rheumatoid Arthritis: FINCH 3 52-Week Results
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Introduction: Filgotinib (FIL) is a potent, selective, oral JAK1 inhibitor. FINCH3 assessed FIL efficacy and safety in methotrexate (MTX)-naive patients with rheumatoid arthritis (RA): Week 24 primary outcome results were previously presented.1 Here we report FINCH3 (NCT02886728) results through Week 52.

Methods: This global, phase 3, double-blind, active-controlled study randomised MTX-naive patients with moderately to severely active RA according to ACR 20/50/70 criteria to FIL 200mg once daily (QD) + MTX <20mg weekly (QW), FIL 200mg QD + MTX, FIL 200mg QD monotherapy + placebo, or placebo + MTX >20mg QW up to Week 52. Comparisons at Week 52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities.

Results: Of 1249 treated patients, 975 received study drug through Week 52. FIL efficacy was sustained up to Week 52. Proportions of patients achieving ACR20/50/70 (%) were increased with treatment with FIL 200 mg + MTX (n = 416; 75.0/62.3/47.8); FIL 100 mg + MTX (n = 207; 73.4/59.4/40.1); and FIL 200 mg monotherapy (n = 210; 74.8/61.4/45.2) versus MTX (n = 416; 61.8/48.3/29.8). FIL 200mg + MTX and FIL 100mg + MTX, and FIL 200mg monotherapy also increased proportion achieving clinical disease remission by DAS28 (CRP) <2.6 (57.4/48.3/35.3); SDAI (31.1/28.8/23.0); and Boolean criteria; improved HAQ-DI; and halted radiographic progression versus MTX alone. Safety was consistent with Week 24 data. Safety outcomes through Week 52 for FIL 200 mg + MTX, FIL 100 mg + MTX, FIL 200 mg monotherapy, and MTX (%) were: adverse event rate 76.4, 79.2, 68.1 and 73.3; serious adverse events 6.3, 6.3, 8.1 and 6.7; serious infections 1.2, 1.4, 2.4 and 1.9; herpes zoster 1.4, 1.4, 1.9 and 1.0; VTE 0, 0, 0 and 0.0; MACE (adjudicated) 1.0, 0.5, 1.0 and 0.5; malignancy 0.2, 0.0, 0.0 and 0.0; and death 0.7, 0.5, 0.0 and 0.0.

Conclusion: Efficacy of FIL 200mg + MTX, FIL 100mg + MTX, and FIL 200mg monotherapy was sustained through Week 52, with faster onset of and consistently numerically greater efficacy for FIL 200mg versus FIL 100mg. No new safety signals were observed.

Reference

P 17
Filgotinib provided rapid and sustained relief of pain and fatigue and improved health-related quality of life in patients with rheumatoid arthritis and inadequate response to biologic DMARDs: Results from the FINCH3 Study
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Introduction: EULAR guidelines recommend a treat-to-target approach focusing on reducing inflammation to prevent joint damage, physical disability, and mortality.1 However, patients consider pain and fatigue reduction, maintenance of physical function, and improvement in health-related quality of life (HRQoL) important.2 In the FINCH2 study, filgotinib (FIL) — an oral, selective Janus kinase 1 inhibitor—in combination with conventional synthetic (cs) DMARD significantly improved signs and symptoms of rheumatoid arthritis (RA) in patients with an inadequate response to a biologic DMARD (bDMARD-IR) compared with placebo (PBO).3

Methods: Patients in this double-blind, randomised study (NCT02886736) received FIL 200mg, FIL 100mg, or PBO while continuing csDMARD therapy. Patient reported outcomes (PROs) were collected prospectively for assessment of pain (VAS pain scale), fatigue (FACTIT-Fatigue), and HRQoL (SF-36). Changes from baseline for each PRO at each time point up to Week (W) 24 were analysed.

Results: 448 patients were randomised and treated (FIL 200mg, n = 147; FIL 100mg, n = 153; PBO, n = 148); 381 (85.0%) completed the study. Baseline mean (SD) VAS pain scale was 67 (21.0), SF-36 physical component summary (PCS) was 31.1 (7.89), SF-36 mental component summary (MCS) was 44.3 (11.6), and FACTIT-FACT-fatigue score was 40.4 (16.6); baseline values did not vary between treatment groups. Significantly greater improvements in VAS pain scores began at W2 and were maintained through W24 for patients on either dose of FIL vs PBO. FIL 200mg significantly improved patients’ fatigue at W4, W12, and W24 compared with PBO, and at W4 and W12 for those on FIL 100mg. HRQoL related to physical functioning (SF-36 PCS) was significantly enhanced at W4, W12, and W24 with both doses of FIL versus PBO. Improvements to mental-health-related Qol (SF-36 MCS) were reported for FIL as early as W4 and maintained through W24, statistically significant improvements at W4 and W12 for FIL 200mg vs PBO.

Conclusion: In a bDMARD-IR patient population with refractory disease and significant disease at baseline, FIL treatment—coadministered with csDMARD therapy—was able to provide rapid and sustained improvements in key measures of pain, HRQoL, and fatigue as reported by patients.

References

P 18
Characterisation of Depth of Response, Including 50% Improvement in ACR Components at Week 12 and Remission at Week 24, Following Treatment with Filgotinib Compared with Methotrexate or Adalimumab in Patients with Rheumatoid Arthritis
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Introduction: Filgotinib (FIL) an oral, potent, selective JAK1 inhibitor showed favourable efficacy at week (W)12 and W24 of treatment for rheumatoid arthritis (RA) compared with methotrexate (MTX) monotherapy (mono) in FINCH3 (NCT02886728) and with placebo (PBO) or adalimumab (ADA) in FINCH 1 (NCT02288796).50% clinical improvement from baseline at W12 is a key checkpoint for RA treatment.1 These post hoc analyses evaluated FIL treatment effect on improvement in ACR components at W12 and remission at W24 in FINCH 3 and FINCH 1.
Methods: FINCH 3 and FINCH 1 were global, phase 3, double-blind studies in patients (pts) with active RA. In FINCH 3, MTX-naïve pts were randomised 2:1:1:2 to once-daily (QD) oral FIL 200 mg + weekly MTX, FIL 100 mg + MTX, FIL 200 mg mono + PBO, or PBO + MTX mono up to W52. In FINCH 1, pts with inadequate response to MTX (MTX-IR) on a background of stable MTX were randomised (3:3:2:3) to oral FIL 200 or 100 mg QD, subcutaneous ADA 40 mg Q2W, or PBO up to W52. Post hoc analyses evaluated proportions of pts with 50% improvement from baseline in each ACR component and in all 7 ACR components (ACR50c) at W12, and proportions of pts with ACR50c at W12 achieving clinical remission at W24. Comparisons between treatments were not adjusted for multiplicity; subgroup comparisons are descriptive.

Results: 1249 pts in FINCH 3 and 1755 pts in FINCH 1 were analysed. A greater proportion of pts (%) in FINCH 3 and FINCH 1 receiving FIL 200mg+MTX (26.2 and 18.5, respectively), FIL 100mg+MTX (19.3 and 12.5, respectively) and FIL mono (22.9, FINCH 3) vs MTX mono (6.0, FINCH 3) or PBO+MTX (2.5, FINCH 1) achieved ACR50c at week 12 (p <0.001). A numerically higher proportions of pts on FIL 200 mg+MTX vs FIL 100 mg+MTX (both studies) or ADA + MTX (FINCH 1) achieved ACR50c and individual components at week 12. Proportions of pts achieving CDAI ≤2.8 or Boolean remission at W24 were higher for pts with vs without ACR50c at W12.

Conclusions: In MTX-naïve and MTX-IR pts with RA, FIL treatment was more effective vs MTX (FINCH 3) or PBO (FINCH 1) for achieving ACR50c at W12—a potential predictor of remission at W24. Proportions of pts achieving ACR50c at W12 were numerically higher for pts receiving FIL 200 mg + MTX vs FIL 100 mg + MTX (both studies) or ADA + MTX (FINCH 1).

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COVID-19 driven care changes in high risk patients from an outpatient to a community setting - a quality improvement survey

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Background: COVID-19 has led to a change in care for patients with chronic conditions, involving a transfer of drug administration from an outpatient to a community setting.

Aim: To investigate patient preferences for treatment settings in the light of the current pandemic.

Methods: Patients, who prior to the pandemic had attended two different outpatient clinics in a university hospital for their infusions or injections, were interviewed by telephone. The semi-structured interviews were analyzed using qualitative and quantitative methods.

Results: Of the 49 participants with either anti-inflammatory or immunomodulatory treatments, 49% switched from subcutaneous injections in the hospital to the community setting, 36.7% from intravenous infusions in the hospital to subcutaneous administration at home and 14.3% moved to intravenous infusions at home. During the pandemic 80.9% wanted to continue their treatment at home, but post the pandemic 46.8% were opting to go back to the hospital. Some practice settings were highly favoring drug administration in hospital. Qualitative data showed that patients while emphasizing the importance of the relationship with the healthcare team had increased concerns about safety because of COVID-19.

Conclusions: The pandemic introduced changes in care in our highly specific patient group, some of which might be positive. The COVID-19 pandemic served as a mirror in which we were able to review and reflect on our model of care. Asking patients about their preferences, including drug application setting, providing self-management support but also monitoring effectiveness and side effects, should be continued during a crisis and beyond and warrants long term follow-up.

P 20

Ultrasound lesions associated with of hydroxyapatite rheumat-isms in the shoulder

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Background: Calcifications (due to BCP crystal deposition) are a common finding in patients with acute inflammatory episodes but also chronic shoulder pain. Ultrasound is a well suited tool for the detection of such calcifications but also for all the associated lesions that could be responsible for the symptoms.

Objective: The goal of the study was to compare the echographic characteristics of patients with BCP calcifications in the rotator cuff and shoulder pain to those with no signs of calcification.

Methods: In this retrospective transversal case-control study of 465 patients with shoulder pain, 125 patients with rotator cuff calcification (RCC) were compared to 120 patients without calcification randomly extracted from the same registry. Subgroups were defined according to the type and the duration of symptoms (Hyperacute painful shoulder, subacute inflammatory symptoms and chronic mechanical pain). The frequency and the types of associated lesions were compared between the two groups according to these different clinical presentations. The aspect of the calcifications were also analyzed in relation with the different clinical presentations.

Results: More than a 1/3 of the patients with calcifications (35% in chronic and 43% in acute symptom groups) had no other echo graphical lesions compared to < 5% of patients without calcification. Calcifications were rarely associated with partial or total rotator cuff rupture (< 10% against > 20% without, p: 0.007). Arc shaped calcifications with LEs were rarely found in acute flares. Most calcifications in hyperalgesic shoulders were either soft without shadowing suggesting a calcification already in the course of dissolution or heterogeneous with some cysts suggesting a partial dissolution of the calcification.

Conclusions: Lesions of the rotator cuff are significantly less frequent in patients with shoulder pain associated with calcification than without especially tendon ruptures. Ultrasound aspect of the calcification suggest the type of symptoms.
Transitional care in Rheumatology: Current practice in Switzerland

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Most children with rheumatic diseases need ongoing medical care during adolescence and adulthood. A good transition into adult rheumatology is needed. About half of the rheumatologists were satisfied with their current evaluation within the network of pediatric and adult rheumatologists. A good transition into adult rheumatology is necessary. Switzerland; 15Department of rheumatology, Cantonal Hospital St. Gallen, Switzerland; 19Department of rheumatology, Cantonal Hospital Winterthur, Switzerland; 20Department of rheumatology, University Hospital Basel, Switzerland

The current practice of transitional care (TC) in Switzerland in relation to EULAR/PReS standards and to describe gaps and challenges in following the recommendations. The aim of this study was to assess the current practice of transitional care (TC) in Switzerland in relation to EULAR/PReS standards and to describe gaps and challenges in following the recommendations. All 10 pediatric Swiss rheumatology clinics offering transition service to adult care agreed to participate. In each clinic the responsible pediatric and adult (n = 20) rheumatologist were separately interviewed using a structured manual addressing EULAR/PReS transitional care standards. The number of patients in follow-up in pediatric centers ranged from 50-363 (median 140). Fifteen of 20 rheumatologists reported to have a written procedure for TC. Three pediatric and two adult rheumatologists used a checklist. The start of TC varied between the ages of 11 and 20. Adherence to medication/appointments followed by disease activity and age were rated as important for initiating TC. Topics discussed most often during consultations were vocational issues (n = 17), effects of alcohol and smoking on disease (n = 16), medication (n = 16) and the impact of disease on daily life (n = 16), sexuality, fertility and pregnancy (n = 15). All pediatric teams performed consultations with the patients alone whereas only 2 performed consultations with the parents alone. Only 2 centers had a TC coordinator. Slightly more pediatric (70%) than adult (60%) rheumatologists rated their TC process as good/very good. Only half of the adult, but all pediatric rheumatologists evaluated support provided for self-management skills of the adolescents as good/very good. None of the physicians carried out formal evaluations of their TC, including patient satisfaction. The main barriers identified for further development of local TC included lack of funding and staff. The current practice of TC in Swiss rheumatology centers is heterogeneous. About half of the rheumatologists were satisfied with their current practice, although no structured evaluation was conducted. To ensure that patients need and receive sufficient transitional care, a structured evaluation within the network of pediatric and adult rheumatologists is needed.

The non-long-coding RNA HOTAIR regulates P3K/AKT and Wnt pathways in synovial fibroblasts from lower extremities.

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Background: Mechanisms involved in joint patterning of rheumatic diseases remain unknown. The non-long-coding RNA HOTAIR is exclusively expressed in synovial fibroblasts (SF) from lower extremity joints. HOTAIR regulates the epigenetic landscape by modulating H3K27me3 histone marks. Here, we analysed the function of HOTAIR in SF.

Methods: HOTAIR was silenced in knee SF from osteoarthritis (OA) patients by GapmeRs. ChiP-sequencing of H3K27me3 marks and RNA-sequencing were performed in GapHOTAIR and control-transfected SF 48h after transfection (n = 3). Enriched pathways and protein interactions were analyzed using KEGG networks. Regulated genes were confirmed by real-time PCR in SF from OA and rheumatoid arthritis (RA) patients (n = 8). Signaling pathways were studied by Western blotting (n = 5) and by the TOP/FOP reporter system for canonical Wnt pathway (n = 4). The expression of HOTAIR was studied after stimulation with TNF-α in SF (n = 17) and correlated with TNF-α-expression in synovial tissues from RA patients (n = 10).

Results: ChiP sequencing showed 2376 genes with differential expression of H3K27me3 marks between GapHOTAIR SF and controls. Transcripts, which lost the repressive H3K27me3 mark and were overexpressed in GapHOTAIR SF, were mainly involved in the P3K/AKT signaling pathway and in canonical Wnt signaling. From the P3K/AKT pathway, we confirmed the overexpression of FGF6 (p = 0.01) and a down-regulation of FGFR2 and FGFR7 (p < 0.05). Validation of HOTAIR led to an increased phosphorylation of AKT. Regarding Wnt signaling, CTNNB1 was overexpressed (p < 0.01), whereas other genes belonging to the canonical Wnt pathway were down-regulated. Functionally, inhibition of HOTAIR led to a decrease in canonical Wnt signaling (p < 0.01). TNFα stimulation led to a 2.1±0.3 decrease in HOTAIR expression in SF (p < 0.0001) and was inversely correlated with HOTAIR in the RA synovium (r = -0.72; p = 0.02). GapHOTAIR SF were characterized by an impairment in migratory properties (p < 0.0001) and an increase in sensitivity to Fas-induced apoptosis (p < 0.05).

Conclusion: HOTAIR regulates P3K/AKT and the canonical Wnt pathway by epigenetic and transcriptional mechanisms. Downregulation of HOTAIR induces changes in the behavior of SF and might influence the phenotype of chronic arthritis in joints of the lower extremities with implications for disease severity and therapy.

Development and validation of a new patient reported outcome measure for systemic sclerosis: the EULAR Systemic Sclerosis Impact of Disease (ScleroD) questionnaire

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Objectives: Patient reported outcome measures (PROM) are important for clinical practice and research. Given the unmet need for a comprehensive PROM for systemic sclerosis (SSc), the ScleroD questionnaire was developed by a joint team of patients with SSc and medical experts.
This is intended as a brief, specific, patient-derived, disease impact score for research and clinical use in SSc.

Methods: This EULAR-endorsed project involves 11 European expert SSc centers. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in a large observational cohort study. Patients completed the ScleroID and comparators SHAQ, EQ5D, SF36. They also weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation is based on the ranking of the weights. The validation study included a reliability arm and a longitudinal arm, evaluating sensitivity to change at follow-up.

Results: Of the 472 patients included at baseline, 109 patients also had a reliability visit and 113 patients a follow-up visit. 84.5% of patients were female, 29.8% had diffuse SSc, mean age was 54.6 years, and mean disease duration 9.5 years. The highest weights were assigned by the patients to Raynaud’s phenomenon, fatigue, hand function and pain, confirming our previous results. The total ScleroID score showed good Spearman correlation coefficients with the comparators (SHAQ, 0.73; EQ5D 0.48). Patient's global assessment, VAS 0.77; HAQ-DI 0.62; SF36 physical score -0.62; each p <0.001). The internal consistency was good; Cronbach’s alpha 0.866, similar to SS-HAQ (0.88) and higher than EQ5D (0.77). The ScleroID had a very good reliability; intra-class correlation coefficient 0.839 (range 0.608 to 0.788 for the individual items), superior to all comparators. Twenty of 113 patients reported a change in the disease status on follow-up. Sensitivity to change; the standardized response mean was 0.34 for the total ScleroID score and highest for lower GI (0.633) and life choices domains (0.521), superior to all other PROM in this study.

Conclusions: The EULAR ScleroID is a novel PROM designed for use in clinical practice and clinical trials to reflect the disease impact of SSc, showing good performance in the validation study. Importantly, Raynaud’s syndrome, impaired hand function, pain and fatigue were the main patient reported drivers of disease impact.

Clinical correlates and relevance of UCLA GIT 2.0 for esophagitis and indication for esophagogastroduodenoscopy in real-life patients with systemic sclerosis

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Background: The gastrointestinal (GI) tract is frequently involved in systemic sclerosis (SSc). The University of California Los Angeles Scderma Clinical Trial Consortium Gastrointestinal Tract Instrument 2.0 (UCLA GIT 2.0) is validated to capture GI morbidity in patients with SSc. The routine clinical investigation of GI involvement in these patients is not standardized and there is no consensus about when and how frequently an esophagogastroduodenoscopy (EGD) should be performed.

Objectives: The aims of this study were a) to determine, in an unselected, real-life cohort of patients with SSc, whether the UCLA GIT 2.0 could discriminate patients for whom an expert rheumatologist would recommend an EGD and b) to analyze the capacity of UCLA GIT 2.0 to identify patients with erosive esophagitis.

Methods: We selected patients fulfilling the ACR/EULAR 2013 criteria for SSc from the Zurich cohort, having completed at least once the UCLA GIT 2.0 questionnaire. We reviewed the medical charts of SSc patients from 2013 to 2019 and recorded data on EGD. We analyzed by univariable logistic regression several parameters, including UCLA GIT 2.0, considered as potentially associated with 1) the referral to EGD and 2) endoscopic erosive esophagitis.

Results: We identified 346 patients (82.7% female, median age 63 years, median disease duration 10 years, 23% with diffuse cutaneous SSc) that fulfilled the inclusion criteria, who filled in 940 UCLA GIT 2.0 questionnaires. In logistic regression, the UCLA GIT 2.0 total score and some of its subscales (reflux, distention/bloating, social functioning, emotional wellbeing) associated with the referral to EGD, with an odds ratio of 2.27 (95% CI: 1.55-3.32) <0.001 for the total score. We found data on 177 EGD performed in 150 patients. In logistic regression, only esophageal symptoms correlated with esophagitis (OR 2.92, 95% CI 1.29-6.61, p = 0.010), while the UCLA GIT 2.0 score and its subscales did not.

Conclusions: In a real-life setting, UCLA GIT 2.0 subscales (reflux, distention/bloating, social functioning, emotional wellbeing) and total score strongly associated with expert interpretation of gastroesophageal symptoms and consecutive referral to EGD. However, they showed no correlation with esophagitis on EGD. The main clinical association of esophagitis was the presence of esophageal symptoms.


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Sebum Metabolites as Biomarkers for Diagnosis and Staging in Systemic Sclerosis (SSc) and SSc-Associated Interstitial Lung Disease

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Background: Protein biomarkers for systemic sclerosis (SSc) and interstitial lung disease (ILD) associated with SSc are sparse and not yet established in routine care. In fibrotic diseases such as SSc, metabolic processes are altered towards an anabolic state. Therefore, the objective of this study was to assess the potential of serum metabolites as biomarkers in SSc/ILD.

Methods: Matched serum samples of SSc patients and healthy controls (HC) were analyzed. Progressive SSc-ILD was defined as a decrease in forced vital capacity (FVC) of >10%, a decrease in FVC of 5-9% and a concomitant decrease of carbon dioxide diffusion of >15%, or an increase of the extent of lung fibrosis on computed tomography from <20% to ≥20% compared to the previous visit (mean follow-up interval = 14 months (range = 9-20)). Sera of HC, non-ILD SSc and stable vs. progressive SSc-ILD patients (n = 12 per group; total n = 48) were screened for 110 metabolites by targeted liquid chromatography tandem mass spectrometry. For univariate analysis, FDR-corrected one-way ANOVA was used. In multivariable partial least squares discriminant analysis (PLS-DA), variable importance in the projection (VIP) scores ≥2 were deemed significant.

Results: In total, 85 metabolites were detected. Univariate analysis showed differential expression of 1-methyladenosine, L-tryptophan, L-tyrosine, L-leucine and xanthosine (p = 0.077, 0.028, 0.028 and 0.032) between all groups. In PLS-DA, HCs and SSc patients differed in their levels of L-tyrosine and L-tryptophan, while levels of L-threonine, 3-aminoisoouic acid, adenosine monophosphate and xanthosine were changed in non-ILD vs. SSc-ILD patients. Receiver operating characteristic (ROC) analysis of candidates from univariable and multivariable testing resulted in separation of SSc patients from HCs by L-tyrosine (AUC = 0.81 (95%CI: 0.67–0.96)), L-tryptophan (AUC = 0.86 (95%CI: 0.75–0.97)) and 1-methyladenosine (AUC = 0.82 (95%CI: 0.71–0.94)). Progressive SSc-ILD patients were separated from stable patients by their levels of L-isoleucine, L-leucine, adenosine monophosphate, and xanthosine (AUC = 0.83, 0.85, 0.79 and 0.77 (95%CI: 0.66–1.00, 0.70–1.00, 0.80–0.97 and 0.55–0.99, respectively).

Conclusions: This study in SSc(ILD) patients suggests alterations in serum metabolite levels corresponding with the presence and stage of disease, indicating the potential use of serum metabolites as diagnostic or discriminating biomarkers upon further confirmation in larger multicenter studies.

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The Hospital Anxiety and Depression Scale in patients with systemic sclerosis - a psychometric and factor analysis in a monocentric cohort

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Background: The Hospital Anxiety and Depression Scale (HADS) is a screening tool used in patients with different medical conditions. However, its validity, reliability and responsiveness in systemic sclerosis (SSc) patients has not been evaluated yet.

Objective: To evaluate the feasibility, validity, reliability and responsiveness of the Hospital Anxiety and Depression Scale (HADS), and to analyse its model structure in patients with systemic sclerosis.
Methods: In this study, 307 systemic sclerosis patients were included. Of these, 90 participated in the responsiveness analysis. An exploratory and confirmatory factor analysis was performed to examine the structure of HADS. Psychometric properties were tested in analogy to the Outcome Measures in Rheumatology (OMERACT) filter.

Results: The exploratory and confirmatory factor analysis revealed that for our population of SSC patients, the HADS model with two sub-scales, HADS-A and HADS-D, and a general scale HADS-S, measuring anxiety, depression, and distress, respectively, was the most appropriate. The HADS showed adequate feasibility, adequate face and content validity and moderate to very strong construct validity (Spearman’s ρ: HADS-A = 0.69 to 0.75 with Sense of Coherence-13, r = -0.72 to -0.86 with the Short Form-36 – Mental Health – Subscale, and r = 0.44 to 0.62 with the Scleroderma Health Assessment Questionnaire). A very good to excellent internal consistency reliability (Cronbach’s α = 0.85 to 0.91, split-half reliability χ = 0.87 to 0.92) was detected. There was no ceiling or floor effect observed and missing answers represented only 0.93% to 2.22% of all answers. In the responsiveness analysis, the HADS showed large to very large effect sizes for worsening of intestinal disease, pulmonary hypertension, modified Rodnan skin score and European Scleroderma Group Activity Index 2001. The rates of anxiety, depression, mixed anxiety-depressive disorder (MADD) and distress identified in our cohort by HADS were 32.7%, 26.1%, 18.6%, and 49.7%, respectively. With the exception of limited cutaneous SSC patients who were more affected than men and patients with diffuse cutaneous SSC, respectively.

Conclusion: The psychometric properties of the HADS make it useful for screening in SSC, where anxiety, depression, MADD, and distress represent a significant burden to patients.

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Awareness of osteoporosis and presence of risk factors associated with osteoporosis among Swiss rheumatology patients

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Introduction: Bone fractures associated with osteoporosis not only impact patients’ quality of life, but also the limited financial resources of the health care system. Due to their expertise in musculoskeletal disorders and patients with predisposing medical conditions, rheumatologists are well positioned to promote diagnosis and treatment of osteoporosis. Adequate awareness of osteoporosis among rheumatology patients is therefore relevant for the prevention and effective management of this disease.

Material and Methods: Our nationwide Bone Health Awareness survey was conducted with specifically designed physician and patient questionnaires covering the prevention, diagnosis and treatment of osteoporosis. Questionnaires were distributed to various specialists across Switzerland, in the language of each region. Completed questionnaires were collected within a single week and analyzed by an independent biometric institute.

Results: Rheumatologists were with 17% the second biggest surveyed physician population after GPs, followed by gynecologists and endocrinologists (n = 262). Compared to total survey population (n = 9065), most rheumatologists were on osteoporosis treatment (23.3% vs. 14.5%) or qualified as potentially at risk. Rheumatologists rated the importance of osteoporosis for their daily practice highest of all surveyed physicians. However, only 41.6% of rheumatology patients were aware of the chronic nature of osteoporosis, slightly above-average in our sample. Presence of lifestyle-related risk factors was similar as in the total survey population. With twice as many rheumatology patients being diagnosed with inflammatory rheumatic disease, a greater proportion was treated with glucocorticoids, thus increasing their risk of developing osteoporosis. While their family history of hip fractures was only slightly higher, rheumatology patients more often reported feeling insecure while walking or afraid of falling, and concerning about bone fragility. 28% of rheumatology patients reported taking calcium and vitamin D vs. 19.7% of all answers. In the responsiveness analysis, the HADS showed large effect sizes for worsening of intestinal disease, pulmonary hypertension, modified Rodnan skin score and European Scleroderma Group Activity Index 2001. The rates of anxiety, depression, mixed anxiety-depressive disorder (MADD) and distress identified in our cohort by HADS were 32.7%, 26.1%, 18.6%, and 49.7%, respectively. With the exception of limited cutaneous SSC patients who were more affected than men and patients with diffuse cutaneous SSC, respectively.

Conclusion: The psychometric properties of the HADS make it useful for screening in SSC, where anxiety, depression, MADD, and distress represent a significant burden to patients.

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Risk Factors for Fractures and Bone Loss after Denosumab Discontinuation: A Real-World Observational Study.

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Background: Denosumab discontinuation without subsequent treatment with Bisphosphonates (BP) is associated with bone loss and multiple vertebral fractures.

Objective: Identifying risk factors for bone loss and vertebral fractures after denosumab discontinuation.

Methods: A total of 227 patients with osteoporosis who discontinued treatment with denosumab and received subsequent treatment with zoledronate, other BPs or Selective Estrogen Receptor Modulator (SERM) or no off-treatment were analysed regarding fracture rate, longitudinal Bone Mineral Density (BMD) changes and Bone Turnover Markers (BTM). Linear regression analyses evaluated loss of BMD and age, BMI (kg/m2), treatment duration, pre-treatment, prior fracture state, baseline T-scores, use of glucocorticoids or aromatase inhibitors and BMD gains under denosumab therapy.

Results: 173 patients received zoledronate after denosumab discontinuation, 30 had no subsequent treatment and 24 received other therapies (other BPs or a SERM). After denosumab discontinuation, zoledronate was associated with fewer vertebral fractures (hazard ratio 0.15, p = 0.014) and all off-treatment therapies retained BMD at all sites. Higher BMD loss was associated with younger age, lower BMI, longer denosumab treatment, lack of prior antiresorptive treatment and BMD gain under denosumab treatment. BTM levels correlated with treatment duration and bone loss at the total hip, but not the lumbar spine.

Conclusions: Zoledronate is associated with fewer vertebral fractures after denosumab discontinuation. Further, BMD loss depends on denosumab treatment duration, age, prior BP therapy and BMD gain under denosumab therapy, whereas BTM levels are associated with bone loss at the total hip and denosumab treatment duration.

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“Inflammaging” and bone in the OsteoLaus cohort

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Background: “Inflammaging” is a coined term that combines the processes of inflammation (within the normal range) and aging, since chronic, low-grade, systemic inflammation emerges with increasing age. Unlike high-level inflammation, with which deleterious effects on bone no longer need to be demonstrated, it is unclear whether inflammaging exerts deleterious effects on bone too.

Method: We assessed associations between inflammaging — measured via cytokine levels (high-sensitivity Creactive protein (hs-CRP); interleukin-1β (IL-1β); interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α)) — and bone parameters (prevalent and incident fractures, bone mineral density (BMD) and trabecular bone score (TBS)) in 1390 post-menopausal women from the OsteoLaus study.

Results: Mean ±SD age was 64.5 ± 7.6 and mean bone mass index (BMI) 25.9 ± 4.5 kg/m2. Median hs-CRP, IL-1β, IL-6 and TNF-α were 1.4 pg/ml, 0.57 pg/ml, 2.36 pg/ml and 4.82 pg/ml, respectively. In total, 10.50% of the participants had a prevalent, low-impact fracture; and, after applying a follow-up, 5.91% had an incident, low-impact fracture. Mean T-score BMD was -1.09±1.53 for the spine, -1.08±1.02 for the femoral neck, and -0.72 ± 0.96 for the total hip. Mean spine TBS was 1.320 ± 0.10. We found a positive association between hs-CRP and BMD at all sites, and between hs-CRP and the TBS, but none of these associations...
ciations were significant after adjustment. We found no association between prevalent or incident fractures and hs-CRP. No association was found between IL-1β, IL6 and TNF-α and BMD, TBS or fractures.

Conclusion: Our results suggest that bone imaging and structure parameters are not associated with the low-grade cytokine levels (within the normal range) observed in inflamming.

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Bone Health in Patients with Rheumatoid Arthritis in a Swiss Cohort
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Introduction: The effect of rheumatoid arthritis (RA) on bone mineral density is well known; however, data from Switzerland has not been yet studied, and the link between RA treatments and their impact on BMD is not clear. We analysed data from the Swiss Clinical Quality Management (SCQM) cohort, which is a database of a large national cohort of patients with inflammatory arthritis.

Patients and methods: We analysed all RA patients included in the cohort between September 1997 and April 2019. We included patients who had a dual x-ray absorptiometry (DEXA) scan during the 12 months preceding a SCQM consultation. Clinical characteristics such as age, gender, body mass index (BMI), disease duration, smoking and alcohol use, inflammatory markers with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), disease activity score (DAS-28), functional status assessed with the health assessment questionnaire (HAQ), rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) and medication use were analysed. These were compared between osteoporotic and non-osteoporotic patients, osteoporosis being defined as a BMD value < -2.5 DS or the presence of an atrophic fracture regardless of the BMD.

Results: Out of the 2675 patients with RA, 2256 had a DEXA scan in the previous 12 months, of whom 614 patients (27.2%) had osteoporosis. The mean age was 60.5 years at the time of the BMD measurement, and 80.4% of patients were female. Patients with OP were significantly older, had a lower BMI, a longer disease duration, a higher CRP and a positive rheumatoid factor, and they were more likely to be smokers, to have had previous corticosteroid treatment with prednisone and to have had a longer exposure to anti-TNF agents. After adjustment for age, BMI, disease duration and CRP, the association between anti-TNF treatment and OP was not significant (p = 0.804).

Conclusion: Prevalence of OP in our patients with RA included in the SCQM cohort was high (27.2%). Characteristics of our Swiss patients were similar to those of international cohort1,2. The main strength of the study was the size of the cohort and its main limitation the extent of missing data. A longitudinal study is currently ongoing on the relationship between RA and the evolution of bone health.

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Losing Face
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Case report: We report an 80-year-old man who presents since 2 years a non-painful deformation of his skull. He is an Italian man, retired mechanic, with a medical history of NID Diabetes, hypertension, dyslipidaemia ans basocellular carcinoma. He takes currently aspirin, antihypertensive and hypolipemiant drugs. CT-scan revealed polyostotic lesions of the skull with an extension to the maxillofacial area corresponding to a grotesque osteolysis. His blood values showed normal PO4-Ca metabolism, normal WBC/RBC count. Liver and renal function were preserved. Biopsy was performed showing ec-tastic vascular structures, with no tumoral cells. Diagnosis of Gorham Stout disease was made based on exclusion of other lytic bone diseases. Concomitantly, the patient mentioned that since 2 weeks he had problem to adjust his denture plate. He showed a mass growing in the palate – evolving very fast and biopsies confirmed a spindle cell osteosarcoma of left maxillary sinus and hard palate. Because the tumor was growing so fast, surgical hemimaxillectomy was performed followed by adjuvant radiotherapy. The clinical course was complicated by a hemorrhage two month later followed by a new hemimaxilllectomy in emergency. The patient is still recovering. We concluded a Gorham stout disease as para-neoplastic syndrome in osteosarcoma. This has never been described before at our knowledge.

Background: The “Vanishing Bone Disease” is rare and the aetiology not well understood. A few studies suggest a combination of factors including the proliferation of abnormal lymphatic vessels coupled with osteolysis. The patients are usually young – children most of the time. The prognosis varies a lot; depending on the site involved. Diagnosis is challenging because there is no specific investigations, it is based on radiological and histopathological features after the exclusion of other bone diseases.

Objective: To report the first case of paraneoplastic Vanishing bone Disease. Conclusion: This case is important to report because there are very few cases of Gorham Stout disease in the literature and it shows a very unusual phenotype of Gorham Stout Disease. The association with osteosarcoma was never described before and this might open a window in the understanding of the pathophysiology.

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Relapsing polychondritis and ulcerative colitis
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Introduction: Relapsing polychondritis is a rare immune-mediated condition characterised by episodes of inflammation of cartilage, particularly of the ears, nose and laryngotracheobronchial tree. In approximately one third of patients, it is associated with another systemic disease. We present here a rare case of relapsing polychondritis associated with ulcerative colitis.

Case report: A man born in 1972 was diagnosed with ulcerative colitis at the age of 45. He was first treated with Prednisone, Budesonfalk and Mesalazina. After a myocarditis imputed to Mesalazine, the treatment was changed for Entyvio then Infliximab. Eighteen months later, he developed an asymmetric polyarthritis treated with Prednisone 60mg in a degressive pattern with favorable course. Under Prednisone 25mg, he presented a chondritis of the right then left auricles which responded well to prednisone increase (50mg per day). The right chondritis relapsed with prednisone withdrawal (30mg per day). Prednisone dose was then re-increased and tapered slower. To date, evolution is good without additional treatment.

Discussion: Relapsing polychondritis (RP) is a clinical diagnosis. Even though the elastic cartilage of the ears is most often concerned, all types of cartilages can be affected. Other organs may be involved including eyes, skin, vascular system and kidneys. Pathogenesis of RP is unknown. The hypothesis is an autoimmune reaction against antigen primarily found in cartilages, in patients genetically predisposed. An inciting event (tissue injury, infection) may expose tissue antigens and generate an excessive inflammatory response. In our case, an arthroscopy of the knee could have been an inciting event. About half of patients develop antibodies to collagen type II, IX, XI or to Matriuin-1, all components of cartilage. The frequency of HLA-DR4 is increased in patients with relapsing polychondritis.

Conclusion: The frequent association of RP with other autoimmune diseases – in our case with ulcerative colitis – suggests an autoimmune mechanism. However, the pathogenesis remain unclear, partly due to scarcity of the disease.

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Extrapyramidal symptoms (ES) with leflunomide therapy: a case study
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A 50-year-old farmer presented with pain and muscle weakness, especially of thigh, shoulder and arm muscles. Under the suspected diagnosis
of polymyalgia rheumatica, the patient received prednisolone from January 2019. Due to lack of response to therapy, further investigations were carried out (including extensive autoantibody diagnostics, protein electrophoresis, HBV, HCV, HIV screening, chest X-ray, abdominal sonography and MR angiography of the aorta). However, the aetiology remained unclear. Due to debilitating symptoms, therapy was first converted to methotrexate in August 2019 and subsequently to leflunomide in October 2019 because of lack of response. 5 weeks following leflunomide therapy, the patient presented with myoclonial as well as choreatic movements of the arms. Furthermore, there was a new onset of Parkinsonian syndrome with rigor, increased muscle tone and initiation disorder with small-step gait. Cranial MRI excluded a (sub)acute ischemia, including the basal ganglia. There were no signs of an infectious/autoimmune etiology in the lumbar puncture and the EEG was inconspicuous. In addition, systemic diseases including Wilson’s disease, hyperthyroidism and syphilis infection were excluded. Due to the association between the occurrence of the ES and the start of leflunomide, drug toxicity was suspected and leflunomide was stopped. In order to increase the metabolism of leflunomide and reduce its half-life of 4 weeks, colestyramine was used. Within one week the ES subsided, however the muscle pain increased significantly in intensity.

**Discussion:** Although it is well known that leflunomide can lead to peripheral neuropathies, recent literature has not been able to demonstrate ES side effects following therapy with leflunomide. Nevertheless, due to correlation of start of leflunomide therapy and onset of symptoms as well as the prompt improvement after discontinuation, we assume that these side effects are associated to leflunomide. A serotonin syndrome might explain the ES, as leflunomide inhibits the MAO. Especially since the accompanying headaches, tachycardia and stool irregularities of the patient stopped after discontinuation of leflunomide therapy.

**Addendum:** A PET-CT without immunosuppressive therapy showed myositis (despite repeated normal levels of CRP or muscle enzymes and inconspicuous electroneuromyography). The muscle biopsy confirmed a dermatomyositis.

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