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ABSTRACTS OF THE ANNUAL MEETING OF THE SWISS SOCIETY OF RHEUMATOLOGY

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SGR-SSR: ORAL PRESENTATIONS (BEST ABSTRACTS)

OP 1

Incidence of major adverse cardiovascular events in patients with rheumatoid arthritis treated with JAK-inhibitors compared to bDMARDs: data from an international collaboration of registries (the "JAK-pot" study)

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Background: Results of the "ORAL Surveillance" trial showed higher risk of major adverse cardiovascular (CV) events (MACE) for Janus kinase inhibitors (JAKi) than for TNF-inhibitors (TNFi). Currently, there is limited evidence of the real-world cardiovascular safety of JAKi.

Objectives: To assess the incidence of MACE in rheumatoid arthritis (RA) patients treated with JAKi, compared to other biologic agents in a large multi-country real-world population.

Methods: Patients from 14 RA registers from across Europe, Turkey and Québec (Canada), starting JAKi, TNF-inhibitors or bDMARDs with other modes of action (OMA), were included. MACE comprised strokes, myocardial infarctions and transient ischemic attacks and were attributed to a treatment up to 3 months after treatment cessation (except for rituximab for which it was 1 year), loss of follow-up, death or end of study. Incidence rates (IR) of MACE per 1000 patient-years (PY) with 95% confidence intervals (CI) were computed. Poisson regression, was used to obtain adjusted incidence rate ratios (IRR), with 95% CI. A sub-analysis was performed on patients aged ≥50 years and ≥1 CV risk factor, mimicking the "ORAL Surveillance" trial inclusion criteria (RCT-duplicate cohort).

Results: Over the 50'325 treatment initiations considered in 34'932 patients with a mean follow-up of 2.8 years, 182 incident MACE were reported. Crude incidence was higher for OMA (2.63/1000 PY) than for JAKi (1.76/1000 PY) and TNFi (1.86/1000 PY). The adjusted Poisson regression demonstrated no significant difference in the incidence of MACE between JAKi vs TNFi (IRR = 0.87 (95% CI 0.56; 1.35)), and OMA vs TNFi (IRR = 1.05 (95% CI 0.74; 1.49)). The RCT-duplicate cohort accounted for 38.4% of treatment courses and had a higher incidence of MACE in each treatment group (OMA: 3.75/1000 PY, JAKi: 2.65/1000 PY, TNFi: 3.48/1000 PY). Similarly to the overall population, no significant difference in the incidence of MACE was observed between JAKi vs TNFi (IRR = 0.78 (95% CI 0.44; 1.38)), and OMA vs TNFi (IRR = 0.84 (95% CI 0.53; 1.32)).

Conclusion: In this real-world study, including 14 RA registers and all currently available JAKi in the respective countries, we did not find a significantly higher risk of MACE in RA patients treated with JAKi compared to TNFi. Inclusion of other registers to increase the statistical power and the evaluation of other adverse events such as thromboembolic events, cancers and serious infections are planned.

OP 2

The diffusion-weighted magnetic resonance imaging scrolling artery sign for the diagnosis of giant cell arteritis

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Background: The 3-Tesla, fat-suppressed, T1-black-blood-sequence (T1-BB) is the standard sequence for MRI of the superficial cranial arteries (SCA) in suspected giant cell arteritis (GCA). Its limitations are: long acquisition time; limited availability; need for contrast agents; is performed only if GCA is suspected. In contrast, diffusion-weighted imaging (DWI) is a fast pre-contrast sequence and is part of almost every MRI head. A 4-point-DWI-scale with segmental rating, using 3D-time-of-flight angiography to identify arteries, showed good diagnostic accuracy for GCA (sensitivity/specificity: 75.9% / 94.2%). [1]

Objectives: To evaluate a pattern-recognition approach for reading DWI-MRI head in suspected GCA and to compare the performance of a novice (medical school graduate) versus a vasculitis expert.

Methods: Retrospectively, 156 patients with suspected GCA were included. The novice received 20 min of training. The "DWI scrolling artery sign" (DSAS) was defined as a hyperintense structure demonstrating the course of a subcutaneous vessel when scrolling through the image stack. The DSAS was rated in 4 regions (fronto-parietal, occipital) in images with a b-value of 1000. For T1-BB, the temporal, occipital and posterior auricular arteries were assessed.[2] The clinical diagnosis after ≥6 months of follow-up was the reference standard. Diagnostic accuracy was assessed for DSAS and T1-BB (expert only). Inter-reader agreement (IRA) was evaluated between experts (n = 20) and between expert and novice (n = 156).

Results: 87 patients with and 69 without GCA were included. For the DSAS, sensitivity was 73.6% and specificity 94.2% (expert) and 59.8% and 95.7% (novice), respectively. For the T1-BB, sensitivity was 88.5% and specificity 88.4%. Overall agreement between DSAS and T1-BB was 80% on region level (499/624; kappa(κ) = 0.59) and 86.5% on patient level (135/156; κ = 0.73). IRA between experts was 95% (19/20; κ = 0.90) for DSAS and 90% (18/20; κ = 0.78) for T1-BB on patient level and 91.3% (73/80; κ = 0.81) for DSAS on region level. IRA for DSAS between expert and novice was 87.8% on patient level (137/156; κ = 0.75) and 91.2% on region level (569/624; κ = 0.77).

Conclusion: The DSAS can be evaluated in <1 minute with a good diagnostic accuracy and reliability for GCA diagnosis. The DSAS is easy to assess and has a high specificity of approx.

95% even for non-specialists. DWI can be used immediately in clinical practice for suspected GCA.

References

1 Seitz 2023

2 Bley 2005

OP 3

The burden of arthritis in very early systemic sclerosis – focus on the clinical pattern, laboratory and x-Ray abnormalities

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Objective: Knowledge about arthritis in very early systemic sclerosis (veSSc) is scarce. Our objective is to assess the prevalence of arthritis in patients with veSSc, the clinical pattern and associations with other disease features.

Methods: We analyzed patients with veSSc, defined as presence of Raynaud's phenomenon and/or at least one of puffy fingers, antinuclear antibodies (ANA), abnormal capillaroscopy, not fulfilling the ACR/EULAR 2013 classification criteria for SSc at baseline. We reviewed their electronic records, in order to exclude cases of arthritis of other causes and to collect and summarize data about the clinical arthritis pattern and laboratory parameters (inflammation markers, serology). An experienced rheumatologist in our team reviewed and assessed the conventional radiography exams for presence of bone erosions. Moreover, we investigated associations between arthritis and relevant disease features (Fisher's test).

Results: SSc-related arthritis occurred in 26 of the included 159 veSSc cases, among which 22/159 (13.8%) at baseline. The pattern of joint involvement was in most cases symmetrical, oligo- or polyarticular, affecting mostly the hand- and finger joints, and more rarely proximal- or lower extremity joints. Twenty percent of the patients also had tenosynovitis. Only a minority of patients had elevated inflammatory markers (2/26 CRP, 3/26 ESR) and 23% (6/26) had a positive rheumatoid factor. Four cases had bone erosions not attributed to osteoarthritis. There was only one overlap case with rheumatoid arthritis. In 14/26 patients a treatment with either conventional or biological DMARDs was necessary (main indication arthritis). The presence of anti-centromere antibodies seems to be protective for developing arthritis (p = 0.038, Fisher's test). Other disease features, such as the other specific antibodies, presence of puffy fingers, elevated inflammatory markers or disease duration were not associated with arthritis.

Conclusion: We observed a significant burden of arthritis in our veSSc cohort, similar to its reported point-prevalence in established disease. Arthritis in veSSc is mostly seronegative and non-erosive, having a symmetrical, oligo- or polyarticular involvement, and rare elevation of inflammatory markers. Despite this apparently mild profile, more than 50% of the patients needed treatment with conventional or biological DMARDs. The presence of anti-centromere antibodies seems to be protective for arthritis.

SGR-SSR: POSTERS

P 1

Prevalence and Risk factors of Osteoporosis in a Belgian cohort of lung transplant candidates: The PROgres Study

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Background: Lung transplant (LT) candidates are at high risk of osteoporosis (OP), due to both their respiratory condition and frequent oral glucocorticoids use. However, few is known on the prevalence and management of OP in LT candidates. This study aims to evaluate the prevalence and therapeutic management of OP in LT candidates and to determine the risk factors associated with OP.

Methods: We included 198 patients patients (103 women) among 388 screened for LT at CHU UCL Namur between January 1998 and December 2020. We collected data on bone mineral density (BMD), measured by Dual-energy X-ray absorptiometry (Hologic) at the lumbar spine, total hip and femoral neck, fragility fracture (FF), and OP risk factors along with other factors suspected of affecting BMD such as inhaled (i) glucocorticoids (GCs) use, pulmonary function tests, hypoxemia and pulmonary disorder type.

Results: OP, as defined by BMD values (T-score ≤ -2.5) and/or FF, was observed in 118 patients (59.6%), among which 54 (45.8%) had only a T-score ≤ -2.5, while 36 (30.5%) had only an FF, with predominant vertebral fractures (77.8%). OP patients were older (median [IQR]) (59.0 years [54.2-62.0] vs 57.0 [53.0-62.0]) and had lower body-mass indexes (mean ± SD) 22.2 ± 4.6kg/m² vs 24.3 ± 4.6kg/m² than non-OP.

Seventy-eight OP patients (66.1%) reached the ten-year probability of major osteoporotic fracture intervention threshold. Among them, 53 received only calcium and/or vitamin D and 25 an add-on therapy, mostly a bisphosphonate (n = 23, 92.0%). Thirty-six OP patients (30.5%) were untreated. OP patients was more prevalent in COPD patients (n = 102, 86.4%) than in those with ILD (n = 33, 16.3%) or any other pulmonary diseases (n = 12, 6.1%).

Finally, OP patients used more iGCs, had lower forced vital capacity and severely impaired forced expiratory volume in one second/forced vital capacity ratio. Oral GCs treatment was associated with FF, regardless of the daily dosage.

Conclusions: Most of LT candidates have OP. OP diagnosis before LT in these patients is crucial for a better management of their bone fragility risk after transplantation. GCs use is a major OP risk factor in this category and should raise awareness on related risks of OP.

P 2

Site-specific assessment of spinal radiographic progression improves detection of TNF blocker-associated disease modification in axial spondyloarthritis: longitudinal observational data from the Swiss Clinical Quality Management Registry

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Objectives: To analyse whether time-varying treatment with tumor necrosis factor inhibitors (TNFi) in radiographic axial spondyloarthritis (r-axSpA) has a differential impact on structural damage progression on different spinal segments (cervical versus lumbar spine).

Methods: Patients with r-axSpA in the Swiss Clinical Quality Management cohort were included if cervical and lumbar radiographs were available at intervals of 2 years for a maximum of 10 years. Paired radiographs were scored by two calibrated readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The relationship between TNFi use and progression in the cervical and the lumbar spine was analysed using generalised estimating equation models and adjustment for potential confounding. Radiographic progression per spinal segment was defined as an increase of ≥1 mSASSS unit or by the formation of ≥1 new syndesmophyte over 2 years.

Results: Mean±SD symptom duration was 13.8±9.8 years. Mean±SD mSASSS progression per radiographic interval was 0.41±1.69 units in the cervical spine and 0.45±1.45 units in the lumbar spine (p = 0.66). Prior use of TNFi significantly reduced the odds of progression in the cervical spine by 68% (OR 0.32, 95% CI 0.14-0.72), but not in the lumbar spine (OR 0.99, 95% CI 0.52-1.88). A more restricted inhibition of progression in the lumbar spine was confirmed after multiple imputation of missing covariate data (OR 0.43, 95% CI 0.24-0.77 and 0.85, 95% CI 0.51-1.41, for the cervical and lumbar spine, respectively). It was also confirmed with progression defined as formation of ≥1 syndesmophyte (OR 0.31, 95% CI 0.12-0.80 versus OR 0.56, 95% CI 0.26-1.24 for the cervical and lumbar spine, respectively).

Conclusion: Disease modification by treatment with TNFi seems to more profoundly affect the cervical spine in this r-axSpA population with longstanding disease. Site-specific analysis of spinal progression might, therefore, improve detection of disease modification in clinical trials in axSpA.

P 3

Pulmonary involvement in patients with seropositive and ACPA positive Rheumatoid Arthritis (RA-ILD) – novel screening protocol for early detection of pulmonary involvement

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Seropositive and ACPA positive Rheumatoid Arthritis (RA) is associated with significant cardiovascular and pulmonary comorbidity. However, screening for early detection of pulmonary involvement especially intestitial lung disease (ILD) in patients with seropositive and ACPA positive Rheumatoid Arthritis is not yet established.

We included a total of 51 consecutive patients with a confirmed diagnosis of seropositive and ACPA positive Rheumatoid Arthritis without symptoms for or known cardiopulmonary disease.

For the purpose of this study, we used a noninvasive radiation-free approach to screen for pulmonary, pleural or vascular manifestation of the disease by means of pulmonary function tests (PFT), cardiopulmonary exercise test (CPET), echocardiography and pleuro-pulmonary transthoracic ultrasound (LUS).

The data of 43 patients (mean age 58.5 years, 81.4% female, 93.02% non-smokers) were available for this analysis, as data collection is still ongoing. With an average disease duration of 10.1 years, 34.88 % showed an erosive course with a mean remission of DAS28 ESR 2.3, DAS28 CRP 2.2 or low disease activity (CDAI 6.2, SDAI 6.6), respectively, depending on the used disease activity score.

A reduced forced vital capacity (FVC ≤80%) on PFT was shown in 3 patients (6.98%), a reduced CO-diffusion capacity (DLCOc-SB ≤80%) in 14 patients (32.56%). In 39% of patients, we found noticeable changes in LUS, 23% with a pattern consistent with ILD which was suspected in 13% with changes on LUS and additional PFT.

Other findings included pleural consolidation suspicious for malignancy and pleural effusion on LUS, severe aortic stenosis in bicuspid aortic valve on echocardiography, severe impaired diffusion capacity due to lung emphysema and obstructive lung disease on PFT.

None of the patients showed signs of pulmonary vascular involvement or cardiac ischaemia on echocardiography or CPET.

In conclusion screening of RA-patients for pulmonary involvement with a non invasive, radiation free screening approach may detect a significant number of asymptomatic patients with signs consistent with pulmonary manifestation of rheumatoid arthritis, along with a variety of other cardiopulmonary comorbidities.

P 4

Is there a decreased risk of developing CF arthropathy in CF patients undergoing treatment that targets the F508del mutation?

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Background: Cystic fibrosis (CF) is characterized by mutations within the CFTR (cystic fibrosis transmembrane conductance regulator) gene that result in a defect of the chloride transporter protein in different organs, particularly in the lung. Musculoskeletal symptoms have been reported in up to 29% of CF patients, most frequently as recurrent episodes of mono- or polyarthritis in joints of hands and feet. Potent CFTR modulator therapies targeting the F508del mutation in CF have become available that increase CFTR protein availability.

Objectives: To characterize musculoskeletal symptoms with arthralgias and arthritis in a cohort of consecutive CF patients.

Methods: 25 CF patients were enrolled in this monocentric, prospective, and cross-sectional cohort study. Correlation analyses were performed calculating nonparametric Spearman correlation rank coefficients.

Results: 22/25 CF patients were under CFTR modulator treatment with a mean treatment duration of 13 + 4 months. Arthralgias and myalgias were reported in 48% and 20% of patients, respectively. Arthritis, mainly involving small joints, was clinically detected in 6/25 (24%) patients and confirmed by ultrasound (US) in 3/6 patients. Self-reported myalgias, were significantly associated with the presence of swollen joints (r = 0.7452, p <0.0001), tender joints, (r = 0.6674, p = 0.0003), a positive squeeze test (r = 0.5898, p = 0.0019) and morning stiffness (r = 0.6556, p = 0.0004). Disease activity as assessed by the SDAI was moderate (mean 18 + 3). CCP and rheumatoid factor (RF) were detected in one patient not on CFTR modulator therapy (with PIP synovitis confirmed by US). Two patients on CFTR modulator therapy tested positive for RF. Another patient was seronegative but synovitis was confirmed by US. Of note, longer duration of CFTR modulator therapy was significantly associated with a lower number of tender joints (r = -0.410 p = 0.054), swollen joints (r = -0.400, p = 0.048) and a lower CRP (r = -0.509, p = 0.048).

Conclusion: The current cohort study confirms that musculoskeletal symptoms are frequent in adult CF patients. Self-reported myalgias were significantly associated with arthritis mainly involving small joints. Interestingly, longer duration of CFTR modulator therapy was associated with a decreased number of tender and swollen joints in line with the assumption that amelioration of mucosal airway inflammation may decrease the risk of developing CF arthropathy.

P 5

Heterogeneity in major cardiovascular events assessment between countries participating in an international collaboration of 20 registers of rheumatoid arthritis patients using Janus Kinase Inhibitors (the "JAK-pot" study)

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Background: Industry, regulators, and the rheumatology community have recognised the need for observational pharmacovigilance studies to monitor the safety of new antirheumatic agents which require large number of patients and a long follow up period to evaluate rare drug-related adverse-events (AEs). Registers provide a unique opportunity to understand it in a real life situation. The best strategy is to combine data from those registers to obtain a large sample size to promote earlier and improved detection of (rare) AE.

Objectives: We evaluate how major cardiovascular events (MACE) are assessed in registers in preparation for a collaborative pharmacovigilance analysis, and present preliminary results.

Methods: The "JAK-pot" collaboration includes 20 RA registers. Their principal investigators were sent a structured questionnaire on MACE assessment. We defined MACE as myocardial infarction (MI), stroke, and transient ischemic attack (TIA), whether or not they led to hospitalisation. We present simple descriptive analysis and statistics of the MACE assessment procedures.

Results: All 20 registers provided responses on the MACE assessment procedures. Two registers (10%) do not record AE. In the remaining 18 registers, 18 (100%) record any cardiovascular event, 18 (100%) record MI, 18 (100%) record stroke, 15 (83%) record TIA, 17 (94%) record deep venous thrombosis (DVT), and 17 (94%) record pulmonary embolism (PE). In 1 register (6%), MACE were reported only if it led to drug cessation.

MACE information and percentages of data collection methods can be illustrated in a structured figure. Two registers (11%) provide a reminder to record any AE at each follow-up.

Eight registers (44%) used Medical Dictionary for Regulatory Activities (MedDRA) as their medical terminology dictionary. Three registers (17%) used International Classification of Diseases (ICD-9 and 10). Seven registers (39%) did not use any specific medical terminology dictionary.

Conclusion: Substantial heterogeneity exists concerning MACE assessment between registers. We found many differences regarding methods of data collection. It might be one source of heterogeneity of the incidence rates among the countries, and be taken into account when analysing the safety of JAKi in collaborative studies. For comparative analyses, a common MACE definition and stratified analyses by country are required to account for differential MACE assessment and varying degrees of potential under-reporting.

P 6

Prevalence of posterior segment lumbar enhancement on MRI in axial spondyloarthropathy: a cross-sectional study

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Background: Spinal and sacroiliac involvement is frequent in axial spondyloarthropathy (axSpA); MRI criteria defining structural and inflammatory lesions have been clearly described. However, enhancement of posterior spinal ligaments and zygapophyseal joints may be observed in patients with back pain who undergo contrast-enhanced MRI of the lumbar spine but have no other signs of axSpA. The clinical significance of this enhancement remains to be defined.

Objectives: To compare the prevalence of enhancement of the posterior lumbar spine elements on contrast-enhanced MRI in patients with axSpA, low back pain (LBP) and asymptomatic volunteers.

Methods: This is a retrospective cross-sectional study including patients with axSpA followed in the rheumatology clinic, patients with LBP without features of axSpA and a prospective cohort of volunteers who underwent a clinically-indicated contrast-enhanced MRI of the abdomen or pelvis, did not have back pain based on a questionnaire, and consented to an additional MRI sequence covering the lumbar spine.

Two musculoskeletal radiologists (R1 and R2) reviewed MRI images blinded to patient clinical data. Anonymized contrast-enhanced sagittal fat-suppressed T1-weighted MRI images were independently analyzed. 40 anatomical structures were scored on every MRI, using a Likert scale (0-3): interspinous and supraspinous ligaments, articular recess, joint space, and periarticular soft tissues of bilateral zygapophyseal joints, from L1 to S1 levels. A positive enhancement was defined as a score ≥2 for every structure. A global enhancement score was calculated by summing up all anatomical structures' scores, which were compared between groups.

Results: MRI images of 248 patients (mean age: 51.9 (19.0)) were reviewed, including 77 patients with axSpA (39.6 (12.7)), 88 with LBP (61.5 (19.5)) and 83 volunteers (53.3 (17.0)).

The prevalence of positive enhancement of the posterior elements (median global score [IQR]) for R1 was 62% (13[8.0-20.2]) in the axSpA group, 72% (20[12.0-28.5]) in the LBP group and 73% (26[18-32]) in the control group. For R1 and R2, the difference between groups was statistically significant (p <0.05). Interobserver agreement between R1 and R2 was fair (kappa = 0.43, [0.37-0.49, 95%CI]).

Conclusion: Enhancement of the posterior elements of the lumbar spine is a non-specific finding frequently encountered in individuals without axSpA.

P 7

Alterations in subchondral bone marrow adipocyte size and secreted factors are associated with pathological bone remodelling in knee osteoarthritis

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Background: Subchondral sclerosis and bone marrow adipose tissue (BMAT) lesions are radiographic hallmarks of knee osteoarthritis (OA). Energy supply through lipolysis of bone marrow adipocytes (BMAd) has recently been established as a crucial mechanism to fuel bone regeneration and maintain bone marrow hematopoiesis during energy deficits. It is unknown whether subchondral BMAd may contribute to subchondral sclerosis in OA through a similar mechanism.

Objectives: To determine whether BMAd-derived factors differed as a function of BMAd size and the extent of subchondral bone remodelling.

Methods: Non-sclerotic (NS) and sclerotic (SC) osteochondral tissue chips harvested from femoral condyles during total knee replacement (n = 60, 10 patients) were explanted for 7 days. Adjacent tissues were processed for histological evaluation of BMAd size on Safranin-O-stained sections. Secretion of adiponectin and pro-Collagen-Iα was assessed by ELISA. Free fatty acids (FFA), glycerol and ALP activity were determined by colorimetric assays. Data were normalized for weight and BMAT fraction of explants.

Results: Bone and BMAT fractions were respectively increased and decreased in SC explants. BMAd size was 1.4-fold reduced in NS (1970±198 μm2) vs SC (1393±151 μm2). Secretion of ALP (2.3-fold), pro-collagen-Iα (2.8-fold), FFA (1.5-fold) and glycerol (1.6-fold) was significantly increased in SC explants. Relative reduction in BMAd size was significantly correlated with increased ALP activity (r = −0.64) and reduced FFA levels (r = 0.78). In addition, relative increases in adiponectin and procollagen-Iα were positively correlated (r = 0.75). Tissue explants displaying the largest increase in osteoblast activity and bone formation showed the smallest increase in FFA secretion (ALP vs FFA, r = −0.81), suggestive of higher rates of FFA uptake.

Conclusions: Collectively these data support the new paradigm that BMAd-derived factors may play a previously unrecognized role in regulating pathological bone remodelling in human OA. Elevated fatty acid oxidation, as evidenced by decreased FFA levels, may be an essential energy source to sustain increased bone remodelling and formation. These findings may provide a rationale for evaluating therapeutic effects of drugs acting on lipid metabolism (metformin, incretins) in OA.

P 8

Characteristics and disease course of untreated patients with interstitial lung disease associated with systemic sclerosis in a real-life two-center cohort

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Background: Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc). Current guidelines consider that some patients may not require pharmacological treatment. To date, the characteristics and disease course of untreated SSc-ILD patients remain unknown.

Objectives: To describe disease characteristics and disease course in untreated SSc-ILD patients in two well characterized SSc-ILD cohorts.

Methods: We included SSc-ILD patients from Zurich and Oslo. Patients were classified as treated if they had received a potential ILD modifying drug (immunosuppressive therapy or nintedanib). ILD progression was defined as (i) decline in forced vital capacity (FVC) from baseline of ≥10% or (ii) decline in FVC of 5-9% associated with a decline in diffusing capacity for carbon monoxide (DLCO) of ≥15%, or (iii) start of any ILD modifying treatment during follow-up. Multivariable logistic regression was performed to identify factors associated with non-prescription of a treatment in ILD patients at baseline. Prognostic factors for progression in untreated patients were tested by multivariate Cox proportional hazards regression. Multiple imputation was used to impute missing data in these models.

Results: 386 SSc-ILD patients were included: 287 (74%) were untreated at baseline, 240 of them were included before 2016. Untreated patients were more often women, had a longer disease duration, more frequently a limited cutaneous form and anticentromere antibodies. They had limited extent of lung fibrosis, higher FVC (96±19 % vs. 81±22%) and higher DLCO (69±20 % vs. 58±21). In multivariable logistic regression, anticentromere antibodies (OR: 8.67 [2.82-26.68], p <0.001) was independently associated with no treatment of ILD at baseline. 234 untreated patients were followed-up for a median of 3.4 [0- 12.9] years. The 3-year cumulative incidence of progression was 44.9% [37.8-51.2] without significant difference between patients included before and after 2016. The absence of anticentromere antibodies, a shorter disease duration and extensive lung fibrosis were independent predictors for lung progression in untreated patients.

Conclusion: In the past, a large number of SSc-ILD have been untreated. Contrary to common belief, about 45% of untreated patients showed progression of ILD after 3 years. With the development of effective and safe therapies for SSc-ILD, our results support a change in clinical practice in selecting patients for treatment.

P 9

Influence of immunosuppressive therapy on gastrointestinal symptoms in patients with systemic sclerosis

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Background: The gastrointestinal (GI) tract is frequently affected in systemic sclerosis (SSc), leading to considerable morbidity and even mortality. Currently, there is no disease-modifying treatment available for SSc-related GI involvement.

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

Methods: We selected patients from our centre who met the 2013 ACR/EULAR classification criteria for SSc and had ≥2 visits with completed GIT, with an interval of 12±3 months between visits. We defined the first visit with a completed GIT as baseline visit. Immunosuppressive therapy was defined as exposure for ≥6 months between the two visits to at least one conventional immunosuppressant, biologic agent, or prednisone ≥10mg/d. The study outcome was the GIT score at the follow-up visit. We performed multivariable linear regression with this outcome as dependent variable and immunosuppressive therapy during follow-up, immunosuppressive therapy before baseline, baseline GIT and several baseline parameters selected by clinical judgment as potentially influencing GI symptoms, as independent variables.

Results: We included 209 patients. Baseline characteristics were: 82.3% female, median (IQR) age 59.0 (48.6, 68.2) years, median disease duration 6.0 (2.7, 12.5) years, 40 (19.1%) diffuse cutaneous SSc, median baseline GIT 0.19 (0.06, 0.43). Of these, 71 patients were exposed to immunosuppressive therapy during the observation period: 27/71 methotrexate, 1/71 cyclophosphamide, 17/71 mycophenolate mofetil, 3/71 leflunomide, 3/71 azathioprine, 6/71 glucocorticoids >10mg/d, 16/34 rituximab, 18/34 tocilizumab. Patients on immunosuppressants during the observation period had overall more severe SSc, higher prevalence of treatment with proton pump inhibitors, and tendentially less severe GI symptoms at baseline and follow-up by medical history. In multivariable linear regression, immunosuppressive therapy, lower body mass index, longer disease duration and lower baseline GIT score were significantly associated with lower (better) GIT scores at follow-up.

Conclusion: Immunosuppressive treatment was associated with lower GIT scores, which suggests potential effects of immunosuppressants on GI manifestations in patients with SSc.

P 10

A Different Presentation of Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome mimicking Sjögren's Syndrome

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Tubulointerstitial nephritis (TIN) and uveitis syndrome (TINU) is an uncommon disease identified by two entities: TIN and uveitis [1].

A 55-year-old female patient was referred to our rheumatology clinic for evaluation of dry eyes and malaise. She had a history of unilateral anterior uveitis. Laboratory work-up showed increased creatinine level (2.64 mg/dL), 848 mg proteinuria per day, elevated CRP (109,7 mg/L), increased sedimentation rate (92 mm/1st hour). Ophthalmologic examination revealed anterior uveitis. Schirmer and Tear Break Up Time Tests confirmed dry eyes. Antinuclear antibody screen showed homogenous nuclear pattern with 1:160 titer. Based on increased creatinine level, proteinuria and positive ANA result we performed renal biopsy.It revealed TIN with eosinophilic infiltration. Besides, salivary gland biopsy was performed which didn't show any specific findings. Anti-SSA and anti-SSB were negative as well. After excluding differential diagnosis,TINU syndrome was diagnosed. We commenced prednisolone. ESR and creatinine levels dropped after two weeks. Uveitis went into remission. As a maintenance therapy, we prescribed mycophenolic acid.

This case demonstrated an uncommon clinical presentation compared to other TINU cases, due to sicca symptoms. In the diagnostic approach to TINU syndrome; exclusion of several diseases is necessary as oculorenal involvement might be seen in the course of those diseases.[2] Although Sjögren's might be suspected in this patient with sicca symptoms, salivary gland biopsy and ENA panel weren't compatible with Sjögren's. As there was no granuloma formation in the kidney biopsy, TIN couldn't be attributed to sarcoidosis or Sjögren's. FDG-positron emission tomography also ruled out sarcoidosis. Negative direct immunofluorescence excluded IgG4-related TIN. She also didn't meet the 2019 EULAR/ACR Systemic Lupus Erythematosus classification criteria. Drug related interstitial nephritis was also unlikely as there was no drug history. In conclusion, this TINU case with overlap of symptoms with Sjögren's underlines that TINU might have different clinical features. It points out a new perspective on approaches in uncommon clinical presentations with oculorenal involvement.

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P 11

Risk of SARS-CoV-2 infection following 3-dose homologous BNT162b2 or mRNA-1273 in patients with inflammatory rheumatic diseases

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In an earlier study, we described how patients with inflammatory rheumatic diseases (IRD) who received the mRNA-1273 vaccine had higher anti-SARS-CoV-2 Spike IgG levels compared to those who received the BNT162b2 vaccine (2-dose primary series)[1]. It is unclear if this difference remains significant after the 3rd dose and how it affects the risk of SARS-CoV-2 infection.

The objectives of this study were to assess the effect of 3-dose homologous BNT162b2 or mRNA-1273 vaccination on:

– the anti-SARS-CoV-2 Spike IgG levels up to 180 d post 3rd vaccine dose

– the hazard of testing positive for SARS-CoV-2 within 365 d post 3rd vaccine dose

Patients from the Swiss cohort for IRD patients (SCQM) who participated in the preceding phase of the study were recruited, answered questionnaires via the mySCQM patient app and provided 2 self-collected capillary blood samples after the 3rd vaccination. Included in the analysis were patients who received a 3-dose homologous vaccine and reported no SARS-CoV-2 infection between the 2nd and 3rd vaccination. Samples were tested for anti-S1 levels. For objectives 1 and 2, respectively, mixed effects continuous outcome logistic regression and Cox proportional hazards regression were used. We adjusted for potential confounders at BL (time of 1st vaccination).

After taking into account age, treatment, and previous SARS-CoV-2 infection at BL, the interval between the 2nd and 3rd vaccine doses, and the timing of sample collection in relation to the 3rd dose, the odds of having higher anti-S1 levels were 3.0 times greater (95% CI 1.6 – 5.7; p <0.001) in patients who received 3 doses of mRNA-1273 vs BNT162b2.

Furthermore, patients who received 3 doses of mRNA-1273 had a hazard of testing positive for SARS-CoV-2 within 365 days after the 3rd vaccination that was circa 1.5 times lower (HR 0.68; 95% CI 0.49 – 0.93; p <0.05) compared to those who received 3 doses of BNT162b2, after adjusting for age, treatment, and previous SARS-CoV-2 infection at BL, as well as the interval between the 2nd and 3rd vaccine doses.

In conclusion, following 3-dose homologous vaccination, individuals from the SCQM IRD cohorts who received mRNA-1273 were found to have higher odds of having elevated antibody levels up to 180 days after the 3rd vaccination. In addition, during the Omicron wave, those who received mRNA-1273 had a decreased risk of testing positive for SARS-CoV-2 up to 365 days after the 3rd vaccination.

Reference

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P 12

Intake of Acetaminophen suppresses antiviral humoral immune responses in patients with RA following vaccination with anti SARS-CoV-2 mRNA based vaccines

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Background: Acetaminophen (APAP = paracetamol) may potentially impact vaccine-associated immune responses. Preliminary data suggest that the intake of APAP has been associated with reduced antibody responses to several vaccine antigens. We and others have shown that patients on antirheumatic therapy developed a delayed anti S1 after mRNA SARSCoV-2 vaccines. Different DMARD regimen have been shown to impair the humoral immune response to mRNA SARSCoV-2 vaccines in patients with rheumatoid arthritis (RA) but the effect of APAP (used by patients on demand) has not been explored thus far.

Objectives: To analyse whether the intake of APAP may interfere with antiviral humoral immune responses following two doses of an anti-SARS-CoV-2 mRNA based vaccine in patients with RA on DMARD therapy.

Methods: The RECOVER trial was a non-randomised prospective observational control group trial and enrolled 77 RA patients on DMARD therapy and 21 healthy controls (HC). We performed a posthoc analysis of blood samples taken before the first vaccine dose (T0), two (T1) and three (T2) weeks after the first and second vaccine dose and at 12 (T3) weeks. APAP levels were measured by ELISA. The antibody response (anti-S) to the RBD within the SARS-CoV-2 S1 protein was measured with the Elecsys. The neutralizing activity NT50 was assessed using an HIV-based pseudovirus neutralization assay against Wuhan-Hu-1.

Results: APAP was detected in serum samples from 34/73 (25%) RA patients and in 7/21 (33%) HC (at least at one time point T0, T1 and/or T2). APAP intake in HC did not affect levels of anti-S at any timepoint and all HC developed potent neutralizing activity (NT50 >250) at week 12. RA patients, who tested positive for APAP at T1, showed comparable anti-S levels at T1, T2 and T3 compared to RA patients not exposed to APAP. The detection of APAP at T2 corresponded to lower anti-S levels at T2. The detection of APAP at T2 was associated with a significantly lower SARS-CoV-2 neutralizing activity at T3, compared to patients without APAP exposure (p = 0.04).

Conclusion: A diminished antiviral humoral immune response was observed in RA patients (but not in HC) who were exposed to APAP at the time of the second mRNA vaccine dose, compared to patients without detection of APAP. Our data suggest that the use of paracetamol within the application of the 2nd vaccine dose may impair vaccine-induced immune responses in patients with an already higher risk for blunted immune responses, such as in RA.

P 13

Leucopenia in a patient with severe systemic lupus: no, it is not always lupus

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Patients with systemic lupus erythematosus (SLE) are at increased risk for infections due to the disease itself as well as to the immunosuppressive medication. Rituximab (RTX) is known for inducing lymphopenia and hypogammaglobulinemia, common risk factors for infections, but agranulocytosis seems to be less well recognized as a side effect of RTX.

We report on a rare case of febrile agranulocytosis under RTX treatment. Ms S. is a 38-year-old patient suffering of severe SLE (with neurological, hematologic, musculoskeletal features) and psoriasis, treated with hydroxychloroquine (HCQ) 600mg/d, methotrexate (MTX) 20 mg/w and RTX 2g every 6 months (total dose of 10 g).

She consults the emergency department of a regional hospital after presenting a right axillary abscess for 4 days, treated topically. She reports progressive cutaneous worsening, associated with fever (38.4°C) since 24h hours and low-grade headache. The patient owns pets but had no skin lesions and presented a probable viral lower respiratory tract infection a week before. RTX was last administered a month before the present symptoms appeared.

The patient has a low systolic blood pressure, heart rate is 80 rpm and temperature is 37.5°C; the clinical status (neurological, pulmonary, cardiovascular, abdominal, oral) shows no abnormalities, besides a right axillary phlegmon. Blood tests show normal IgG, IgM and IgA, leucopenia (2.5 G/L), lymphopenia (0.49 G/L), agranulocytosis (neutrophils 0.07 G/L), slightly elevated CRP (33 mg/L) and a good renal function.

Immunosuppressive treatment is suspended, phlegmon surgically evacuated and a broad-spectrum antibiotic therapy introduced, later adapted following microbiologic analysis. Doxycycline sensitive S. aureus was identified in cultures from the abscess. Neutrophil count evolved favourably to Filgrastim administration, rising from 0.07 to 17.1 G/L, and no complications were encountered. Later, HCQ and MTX were re-introduced, RTX dose reduced from 2 to 1g twice a year, strictly monitored by periodic blood tests.

Agranulocytosis under RTX is a rare but highly dangerous complication. In case of confirmed agranulocytosis, close treatment monitoring is mandatory, and the indication and the dose of RTX treatment should be reassessed. Strict recommendations must be formulated to every patient in case of fever or other signs of infection.

P 14

Enthesitis, arthritis and subsequent muscle atrophy, triggered by trauma, as the initial presentation of psoriatic arthritis sine psoriasis

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Case: A 39 year old female patient presented with persistent pain after distortion of her left knee 12 months ago. An initial MRI had revealed a partial rupture of the anterior cruciate ligament. Despite continuous conservative treatment, knee pain and swelling persisted. She developed progressive gait difficulties due to an increasing weakness of the quadriceps muscle and atrophy of the lower thigh. A subsequent MRI showed an enthesitis of the quadriceps tendon, osteitis of the patella and synovitis of the knee. A neurologic evaluation confirmed the inability to fully extend the left knee (M4/5), without electrophysiological correlate. MRI showed an edema signal pattern and contrast enhancement in the lateral and intermedius vastus muscle, along with significant atrophy. Myositis related autoantibodies were negative, the creatine kinase was repeatedly normal. A muscle biopsy taken from the vastus lateralis muscle showed preferential type 2 fibre atrophy, consistent with atrophy related to inactivity.

Two years later, she noticed pain in her forefoot. The clinical examination revealed dactylitis of the 2nd toe and tenderness of the MTP joints. An MRI of the forefoot confirmed synovitis of the MTP joints (Dig II, III) and dactylitis with tenosynovitis of the flexor tendons of the 2nd toe.

With a positive family history for psoriasis, the absence of a rheumatoid factor and the presence of dactylitis, the patient formally fulfilled the CASPAR criteria and we established a diagnosis of psoriatic arthritis sine psoriasis. The patient improved on treatment with glucocorticoids and methotrexate, later guselkumab was added.

Discussion: In our patient, a traumatic injury preceded synovitis of the knee and enthesitis of the quadriceps tendon which led to ipsilateral atrophy of the thigh. Subsequent arthritis of the forefoot and the development of dactylitis led to a diagnosis of psoriatic arthritis. We postulate that the inital trauma triggered this cascade of events. Trauma as a triggering factor for enthesitis and synovitis has been discussed previously within the pathophysiology of psoriatic arthritis ("deep Köbner phenomenon").

P 15

Caution: Is every region of interest imaged in your PET-CT examination?

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We here report on a 67-year-old female patient suffering from adenocarcinoma of the lung, undergoing treatment with the EGFR inhibitor osimertinib. The patient was referred for rheumatologic evaluation due to muscle pain and an elevated creatine kinase (345 U/l, upper limit of normal 145 U/l). Initially, drug-associated myositis was suspected. Because of continuous muscle weakness and pain, myositis associated autoantibodies were screened and revealed TIF1-gamma antibodies. Therefore, paraneoplastic dermatomyositis was suspected.

To evaluate whether remission or progression of bronchial carcinoma had occurred and to exclude a secondary malignancy, the patient underwent a PET CT that did not reveal evidence of tumor progression or myositis. The patient continued to complain about pain and weakness, predominantly in both thighs. It was realized that the standard PET CT protocol applied for detection and monitoring of malignancies in our institution does not include the lower extremities distally from the proximal femur.

As myositis was still suspected, an additional MRI of the thighs was performed and revealed the presence of a lipomatous tumor of the distal femur. It had not been noted during the initial clinical examination nor by the patient. The distal left thigh was not examined in the initial PET CT. Biopsy of the lipomatous mass revealed an atypical lipomatous tumor representing a locally aggressive mesenchymal neoplasm.

This case demonstrates that an underlying neoplasm may be missed even if PET CT as the ultimate diagnostic tool is applied. Depending on the PET CT protocol and clinical suspicion, further diagnostic procedures may be warranted in an individual patient. Ideally, especially when a malignant growth has to be excluded, the PET-CT protocol should be adapted to include all parts of the body.

P 16

RA and pulmonary nodulosis : A diagnostic challenge

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Pulmonary nodulosis is a rare extra-articular manifestation in RA that is probably underestimated. It is often a very challenging diagnosis given all the oncologic, and infectious possible alternative diagnosis.

We present a case of a patient with seropositive RA and an impressive pulmonary excavated nodulosis under methotrexate. Our objective is to discuss the explorations available, their limitations, and to highlight the difficulties we may encounter from a clinical perspective.

P 17

T1-black-blood magnetic resonance imaging of the superficial cranial arteries in giant cell arteritis: semiquantitative scoring outperforms scoring with wall thickness measurements

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Background: The post-contrast, 3-T, fat-suppressed, T1-black-blood (T1-BB) is the reference sequence for MRI of the superficial cranial arteries (SCAs) for suspected giant cell arteritis (GCA).[1] Two different T1-BB scoring schemes are used in clinical practice.[1,2] The original version (Sem-T1-BB) is a semiquantitative visual ordinal scoring scheme.[1] The newer composite version (Comp-T1-BB) has retained the original definitions but added wall thickness thresholds.[2] How to measure SCA wall thickness is not standardized, and with a slice thickness of 3mm, partial volume effects significantly affect measurements. How both scoring schemes compare is unknown.

Objectives: To compare diagnostic accuracy of two T1-BB scoring schemes (Sem-T1-BB vs. Comp-T1-BB) for MRI of SCAs in suspected GCA.

Methods: Retrospectively, 156 patients with suspected GCA were included. The temporal, occipital, and posterior auricular arteries were assessed bilaterally on T1-BB images by vasculitis experts. Both scoring schemes included the following definitions (≥2 considered abnormal): 0, no wall thickening and no enhancement; 1, no wall thickening with slight enhancement; 2, wall thickening with strong enhancement; 3, wall thickening with strong wall and perivascular enhancement.[1] For Comp-T1-BB only, thresholds for wall thickness had to be met: 0, <0.6mm; 1, <0.6mm; 2, ≥0.6mm; 3, ≥0.7mm.[2] The expert diagnosis after a follow-up of ≥6 months was the reference standard. Diagnostic accuracy for scoring methods was compared.

Results: 87 patients with and 69 without GCA were assessed. Measures of diagnostic accuracy for Sem-T1-BB and Comp-T1-BB: sensitivity 88.5%/80.5% (p = 0.008), specificity 88.4%/91.3% (p = 0.16), correct diagnosis 88.5%/85.3% (p = 0.10). Binary agreement on segment level was 91.2% (1127/1236, kappa(κ) = 0.79), but 24.9% (106/425) of pathological segments in Sem-T1-BB were rated normal by Comp-T1-BB. Inter-rater analysis between experts for Sem-T1-BB and Comp-T1-BB (subset of 20 patients): correct diagnosis on patient level 18/20 (90%) for both readers and schemes, κ = 0.78 and 0.79; binary agreement on segment level 89.6% (146/163, κ = 0.79) and 80.4% (131/163, κ = 0.56).

Conclusion: Up to 25% of pathological segments may be missed if wall thickness thresholds are used. Sem-T1-BB is the superior method because scoring is faster, more sensitive and equally specific for the diagnosis of GCA compared to the more complicated Comp-T1-BB.

References
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P 18

Determination of temporal artery ultrasound intima-media thickness cut-off values for the diagnosis of giant cell arteritis using an external segment-level MRI-reference

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Background: The intima-media thickness (IMT) of the temporal arteries (TAs) is increasingly used for diagnosing giant cell arteritis (GCA). Previously, IMT cut-offs were derived using either clinical diagnosis or expert assessment of ultrasound images as diagnostic reference. [1-3] The post-contrast, 3-T, fat-suppressed, T1-black-blood (T1-BB) MRI has excellent sensitivity and specificity for diagnosing GCA. It may be used as an intra-individual external segmental reference standard for the derivation of IMT cut-offs for diagnosing GCA. [4]

Objectives: To derive IMT cut-offs for TAs for diagnosing GCA based on the combined reference standard of T1-BB at the segment level and clinical diagnosis at the patient level.

Methods: Retrospectively, 144 patients with suspected GCA who underwent both ultrasound and T1-BB MRI of the TAs within 7 days were included. TAs were examined with 18-22 MHz probes; the maximum IMT of the compressed segments (common superficial temporal artery (CSTA), frontal/parietal branch) was registered bilaterally. The T1-BB was re-read by vasculitis experts, each segment was scored separately. All segments from patients without GCA and all pathological segments in T1-BB from patients with GCA were used to derive new IMT cut-offs. In addition to the statistically best cut-offs, cut-offs resulting in a specificity of ≥90% on the patient level were selected, since a very high specificity is crucial for diagnosing GCA in daily practice. Diagnostic accuracy of new cut-offs was evaluated with the expert diagnosis after ≥6 months as the reference standard.

Results: 74 patients with and 70 without GCA were assessed. The statistically best cut-offs for unilateral IMT of CSTA, frontal, and parietal branches were 0.43 mm, 0.34 mm, and 0.28 mm, with a sensitivity and specificity of 86.2%/93.1%, 92.3%/88.3%, and 88.8%/83.1% on the segment level, and 86.5%/71.4% on the patient level. Clinically optimal IMT cut-offs were 0.51mm, 0.43 mm and 0.35 mm, respectively, resulting in

an overall sensitivity/ specificity of 75.7%/90.0% for the diagnosis of GCA. For the patient subset with cranial symptoms (81.2%), sensitivity/specificity was 82.5%/94.4%.

Conclusion: The new IMT cut-off values for TAs, based on a combined reference standard (MRI on segment and clinical diagnosis on patient level), can be used for the diagnosis of GCA, with better performance in patients with cranial manifestations.

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4 Bley TA 2005

P 19

Improvement of Sleep Impairment in Patients with Rheumatoid Arthritis Achieving Remission or Pain Relieve with Upadacitinib: Results from the Post-Marketing Observational SLEERA Study

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Background: Sleep impairment is a common clinical condition in the rheumatoid arthritis (RA) population, which has been reported in over 60% of patients. Although few longitudinal studies demonstrated change from baseline on sleep quality with advanced therapies, none of them described the clinical meaningfulness of these changes by subjective (subj.) and objective (obj.) measures.

Objectives: The SLEERA study aims to investigate the impact of upadacitinib (UPA) on sleep quality in a real-world (RW) RA population in Switzerland, by using the Pittsburgh Sleep Quality Index (PSQI), and an actigraphy-based obj. measure.

Methods: SLEERA is a sub-study of UPHOLD, an international, multicenter, prospective, non-interventional, open-label, observational cohort study (NCT04497597) that assesses sleep quality in a RW population of adult Swiss patients (pts) with moderate-to-severe active RA, initiating treatment (Tx) with UPA 15 mg QD. This primary interim analysis reports data for all enrolled pts up to 3 months after Tx start. All data were analyzed as observed, with no imputation of missing data.

Results: Of the 39 pts (87% female) included in this study, 35 completed the follow-up visit at month 3. The mean age and disease duration were 59.5 (13.9) years and 7.0 (8.3) years, respectively. The mean initial DAS28-CRP was 4.1 (1.0). At baseline, 76% of patients showed subj. sleep impairment (defined by PSQI >5) and 51% had obj. poor sleep efficiency (defined by actigraphy sleep efficiency <85%). At month 3, UPA showed significant improvement in the PSQI total score with a decrease of 2.26 (2.92, p value <0.001), as well as other subj. outcomes. The proportion of obj. poor sleepers decreased to 38%, while sleep efficiency and physical activity outcomes in total remained unchanged. However, pts achieving DAS28-CRP remission or absence of pain after 3 months of Tx showed higher improvements in both subj. and obj. measures compared to those who did not achieve DAS28-CRP remission or have residual pain.

Conclusions: In this Swiss cohort, a high proportion of RA pts exhibited sleep impairment. UPA pts significantly improved their subj. sleep quality after 3 months. Higher improvements for both subj. and obj. sleep measures were observed in pts achieving remission or absence of pain. This research provides evidence of sleep impairment in RA pts which can be improved following a Tx, and further supports the importance of remission when assessing disease Tx goals.

P 20

Burden of COVID-19 in patients with inflammatory rheumatic diseases: insights from a Swiss app-based survey

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Background: Patients with inflammatory rheumatic diseases are at risk of infection and severe outcomes with COVID-19. COVID-19 may also affect their quality of life, for example by maintaining protective measures (masking, restriction of social contacts, etc.) while the general Swiss population no longer does. In this study, we investigated factors contributing to a different perception of the burden of COVID-19 among patients with inflammatory rheumatic diseases.

Method: We included all patients registered in the Swiss Clinical Quality Management (SCQM) registry with rheumatoid arthritis (RA), axial spondylarthritis (axSpA), psoriatic arthritis (PsA), undifferentiated arthritis, polymyalgia rheumatica or giant cell arteritis who answered the questionnaire about the extent to which the pandemic is affecting patients' personal and social lives in the mobile My-SCQM app between the 4.11 and 11.12.2022. We performed descriptive analysis on the whole population and characterized them in 5 ordered treatment-subgroups: rituximab > JAK-inhibitors > other b/tsDMARDs > csDMARDs > none of these treatments. The ordered grouping implies that someone taking e.g., both a JAKi and a csDMARD will be assigned to the JAKi category.

Results: There were 1357 respondents, with a median age of 57. 63% of participants were female. 33% are living with children. 36% had RA, 34% had axSpA, 22% had PsA and 8% had another inflammatory rheumatic disease. 100 patients received csDMARDs, 94 JAKi, 18 rituximab, 695 other b/tsDMARDs, and 450 none of these treatments.

COVID-19 affects the general lives of 10% of patients on a scale greater than 7 out of 10. 3% of participants report that COVID-19 impacts their social environment (family and friends) on a scale greater than 7 out of 10.

33% of patients report no fear of COVID-19 after vaccination, however, 27% still report continuing anxiety against the virus. Participants taking rituximab (35%) are more likely to persist in fear than those taking csDMARDs and JAKi (26% and 20% respectively).

More than half of the population reported to still wear masks, with rituximab users most likely to wear them (72%), followed by JAKi takers (65%).

Conclusion: According to our study, even after two years of the COVID-19 pandemic, IRD patients (mainly JAKi and rituximab users) still feel the burden of the disease. Additionally, one out of two IRD patients is wearing facial masks (although they were not mandatory in Switzerland at the time of the survey).

P 21

Feasibility study of an electronic health record-based gout registry

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Background: Gout is the most common inflammatory rheumatism worldwide but remains largely undertreated. To evaluate the current standard of gout care, there is an unmet need for gout registers.

Objectives: To establish an electronic health record(EHR)-based gout registry, to assess the correct identification of gout patients by manual chart review, and to evaluate the objective validity of gout diagnosis based on the ACR- EULAR 2015 gout classification criteria.

Methods: EHR of patients >18 years old consulting between 01.01.2013 and 31.12.2022 at the Geneva University Hospitals, a 2000-beds tertiary hospital that provide in- and outpatient services, were screened based on the presence of at least one of six criteria: ICD-10-GM gout diagnosis, gout-related terms in the list of diagnosis or any patient's documents, prescription of urate-lowering therapy, presence of uric acid crystal in synovial fluid and radiology reports of gout associated damages. 80 charts were randomly selected from the ICD-10, diagnostic list, punctions and drugs queries. The positive predictive value (PPV) to detect a gout was established if a gout diagnosis was found in any part of the EHR. To assess the validity of the gout diagnosis, the 2015 ACR-EULAR gout criteria was scored.

Results: The six criteria identified 10'382 patients suffering from gout. Most patients were detected by the documents and drugs query. A significant number of patients (16.9% outpatients and 24.5% inpatients) were detected by the drugs query without any documented gout diagnosis. PPV were 100% for ICD-10-GM code, list of diagnosis and punction, and 75% for urate-lowering therapy, while PPV based on a combined query was 93.8% to detect a gout patient. 55 patients had at least one documented gout attack and 25 had an antecedent gout. Of the 55 patients with an acute gout, 39 patients (70.9%) had a positive articular aspiration for uric acid or the presence of tophus. The remaining 16 patients (29.1%) had a mean score (SD) of 5.5 (2.39) for the ACR-EULAR 2015 classification (threshold to classify as gout is ≥8).

Conclusion: We demonstrate the feasibility of an EHR-based gout registry, with good positive predictive value and the ability to identify patients without a documented gout diagnosis in their EHR. In a second stage, we will use the registry to evaluate clinical indicator of best practice in gout management.

P 22

Improving fracture prediction in patients with osteoporosis using machine learning techniques: a nationwide, registry-based cohort study

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Objectives: Fracture prediction is essential for the adequate management of patients with osteoporosis. The aim of this study was to analyse the performance of different machine learning models and to identify the most relevant clinical factors for fracture prediction.

Methods: This prospective cohort study analysed a prognostic fracture risk- prediction model using clinical risk factors, T-scores, trabecular bone score (TBS) and treatment information from subjects in the nationwide Osteoporosis Registry of the Swiss Society of Rheumatology. Survival analysis was used to predict the 2-year risk of vertebral, hip and any fractures in a training subset. The C-index was estimated in the test set to evaluate the quality of the model using cumulative or dynamic areas under the curve, and was compared with the performance of state-of-the-art machine learning techniques such as Random Survival Forest and eXtreme Gradient Boosting with an accelerated failure time model. Both Cox proportional hazard model and machine learning models were externally validated using data from the UK biobank.

Results: A total of 15,383 postmenopausal women (mean age 68 ± 9 years) with 26,986 dual-energy X-ray absorptiometry scans and clinical visits were enrolled between January 2015 and October 2022. Of these women, 6,202 were followed-up for a median of 4.1 years [2.7 to 6.0]. During follow-up, 1,227 women suffered a fragility fracture, including 902 fractures within 2 years of follow-up. The C-index for fracture prediction reached 0.68 for vertebral fracture, 0.76 for hip fracture and 0.67 for any fracture, and further increased with longer follow-up periods of up to 7 years. In comparison, the 10-year fracture prediction C-index calculated with FRAX® Switzerland was 0.61 for major osteoporotic fracture and 0.66 for hip fracture. The most important variables in the Lasso-Cox model were age, bone density and previous fracture. In addition, TBS was relevant for vertebral and wrist fractures, while the number of falls was an important predictor of hip and wrist fractures. Performance of both Cox proportional hazard and machine learning models showed similar prediction scores in the UK biobank dataset consisting of 5,474 postmenopausal women with 290 fractures during follow-up.

Conclusions: Fracture risk prediction by FRAX® can be improved by modifying fracture prediction models to include the T-score at the lumbar spine, TBS, number of falls and recent fractures.

P 23

Evaluation of the knowledge of internal medicine physicians, final-year medical students and rheumatologists regarding the diagnosis and management of gout in Switzerland

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Introduction: Gout is the most common inflammatory rheumatism in adults,it is commonly undertreated despite numerous therapeutic options and the availability of international recommendations. To explore the reasons why gout is undertreated, we aimed to assess and compare the knowledge of primary care physicians (internists), rheumatologists, and final-year medical students regarding the diagnosis and management of gout in Switzerland.

Method: We conducted a multicenter cross-sectional study between December 2021 and August 2022. All primary care physicians and hospital internists practicing in academic hospitals in Switzerland, rheumatology specialists, and final-year medical students from all 6 Swiss faculties of medicine were invited to complete an online questionnaire based on recommendations (EULAR and ACR). This multiple choice questionnaire consisted of 28 questions including 68 positive answers (since more than one positive answer was possible for each question). Participants were considered as having responded successfully to the questionnaire with at least 2/3 (45) correct answers.

Results: We received approval for participation from 16 academic hospitals, 4 faculties of medicine, and the Swiss Society of Rheumatology. We included a total of 378 participants: 97 medical students, 210 internists and 71 rheumatologists.Only 33% of final-year medical students demonstrated sufficient knowledge about how to manage gout, compared to 66% of internists and 93% of rheumatologists. 55%, 48% and 14% in the student, internist and rheumatologist groups respectively did not know what type of crystals were found during a gout attack. The majority of participants in the different groups were familiar with at least one of the treatments that should be used for the management of a first acute attack of gout. Most participants in all 3 groups did not know the indications for initiation of hypouricaemic therapy. 80% of students, 62% of internists and 18% of rheumatologists were unaware of the target urate serum level to aim for when introducing hypouricaemic therapy.

Conclusion: These results suggest that knowledge about the diagnosis and management of gout is sub-optimal among final-year medical students and primary care physicians across Switzerland. Although most rheumatologists demonstrated good knowledge about the management of gout, a surprising proportion did not, despite being experts in this field. Knowledge about the gout needs to be improved.

SGR-SSR: BEST CASES

Case 1

Transfusionspflichtige Anämie durch erworbene Faktor II-Defizienz als Erstmanifestation eines Lupus erythematodes mit positiven Antiphospholipid-Antikörpern

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Die 28-jährige Patientin wurde initial durch die Kolleg:innen der Gynäkologie bei ausgeprägter Hypermenorrhoe mit einem transfusionspflichtigen Hämoglobin (Hb)-Abfall auf 6,8 g/dl gerinnungsmedizinisch abgeklärt. In der Gerinnungs- und Immundiagnostik liessen sich eine deutliche Positivität der Antiphospholipid-Antikörper (Beta2-Glykoprotein-AK vom Typ IgG 558 U/ml, Anti-Cardiolipin-AK vom Typ IgG >418 U/ml, positives Lupus anticoagulans), eine verlängerte aPTT (75 s), eine milde Thrombopenie (um110 G/l), ein deutlich verminderter Faktor II (17%, Norm 60-150%), antinukleäre Antikörper (ANA) mit einem Titer von >1:640 (Muster: AC-1 homogen), dsDNA-Antikörper sowie eine ausgeprägte Komplementverminderung von C3 und C4 nachweisen. In der gezielten Anamnese liessen sich keine thrombo-embolischen Ereignisse erfragen, bei unerfülltem Schwangerschaftswunsch auch keine gesicherten Aborte. SLE-kompatible Symptome waren: Polyarthralgien und eine mögliche OSG-Arthritis, eine Alopezie und ein mildes Raynaud-Phänomen. Bei anhaltender Transfusionspflichtigkeit entschieden wir uns zu einer Prednison-Therapie (50 mg/d initial, in absteigender Dosierung). Hierunter zeigte sich eine Normalisierung des Faktors II, ein Anstieg der Komplementfaktoren und rückläufige Titer für die dsDNA-Antikörper, sowie eine Sistierung der Hypermenorrhoe mit konklusiver Stabilisierung des Hb. In Zusammenschau wurde eine erworbene Faktor II-Defizienz mit Triple-Positivität der Antiphospholipid-Tests bei Neudiagnose eines systemischem Lupus erythematodes postuliert, obwohl in einem Mischversuch kein Autoantikörper gegen Faktor II nachgewiesen werden konnte. Unter immunmodulatorischer Therapie mit Hydroxychloroquin konnte in der Folge die Prednisondosis auf <5mg/d reduziert werden, was für eine immunvermittelte Genese spricht. Eine Autoimmunhämophilie als Erstmanifestation eines SLE ist eine Rarität. Die Coexistenz einer Hämophilie und einer Hyperkoagulabilität stellen eine besondere Herausforderung an eine optimale Prophylaxe und Therapie der Patientin, insbesondere bei der möglichen Schwangerschaftsplanung in Zukunft.

Case 2

INTERLEUKIN 1 INHIBITION AND BARICITINIB IN VEXAS SYNDROME, A CASE-PRESENTATION

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Background: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first described in October 2020 (1). It is an adult-onset inflammatory syndromes with a broad spectrum of clinical manifestations, including: dysplastic bone marrow with cytopenias, vacuoles in myeloid precursor cells, skin and pulmonary involvement, polychondritis and venous thromboembolism. Underlying is a somatic mutation affecting the UBA1 gene on the X chromosome, encoding the major E1 enzyme that initiates ubiquitylation (1).

Patient and therapy: We present a case of a 60-year-old man with a multisystemic inflammatory syndrome. He first presented with a Sweet`s syndrome (neutrophilic dermatosis, picture A, B). Three years later, he developed seronegative symmetrical polyarthritis. We changed the therapy from colchicine to adalimumab with partial control of the arthritis, but no efficacy for Sweet`s syndrome. In addition, he developed generalized lymphadenopathy, chondritis nasii and a progressive macrocytic anemia. Because of recurrent thrombembolic events (pulmonary embolism, deep vein thrombosis) anticoagulation with dabigatran was installed. PET-CT scan showed intensive FDG-uptake of the whole skeletal bone marrow (picture C). Subcutaneous injections of anakinra provoced massive local site reactions after two weeks with intense activity on PET-CT scan (picture D). The bone marrow aspirate showed dysplastic changes and vacuoles in the myeloid precursor cells (picture E). Genetic analysis from the bone marrow found a somatic mutation affecting methionine-41 in the gene UBA1 on X chromosome (p.Met41Leu) confirming VEXAS syndrome. Baricitinib treatment did not allow for glucocorticoid reduction below 50 mg of prednisolone equivalent per day. Under the current therapy with canakinumab no injection-site reactions were occured.

Conclusions: VEXAS syndrome should be considered in a middle-aged male with a progressive multisystemic inflammatory syndrome and hematologic disorders. Injection-site reactions are a known adverse event due to anakinra, but the majority are mild (2, 3). Our patient developed a severe delayed injection-site reaction, underlying pathergic phenomenon or a T-cell mediated allergic reaction. Baricitinib was not enough effective as steroid-sparing agent in our case. Overall, januskinase inhibitors should be used with caution in VEXAS syndrome, regarding their potential thrombotic side effects (4).

Case 3

A patient with GCA treated with glucocorticoids and tocilizumab. Is the cure the curse?

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We here report on an 80-year old male patient diagnosed with GCA in 2019, who initially presented with persistent headache following an accident. In addition, he reported morning stiffness of the shoulder girdle muscels of more than one hour. Visual symptoms were absent. Clinical examination revealed tenderness of the temporal arteries and a periarterial halo sign was detected by ultrasound. Laboratory results showed a slightly elevated CRP 19 mg/l and ESR of 24 mm/h. An MRI of the aortic and supraaortal branches was performed that demonstrated involvement of the subclavian, carotid and axillary arteries. Treatment was initiated with prednisone 80mg/daily (1mg/kg). Clinical symptoms improved but reoccurred during prednisone tapering and tocilizumab was added. A few weeks later, the patient presented with severe headache, retrosternal pain and he was pale and sweating. CRP was elevated to 264 mg/l and the patient was hospitalized. As CK and troponin were elevated, dual platelet inhibition was started on suspicion of NSTEMI, but a myocardial scintigraphy showed no signs of ischemia. A thoracal CT scan revealed a mass close to the right hilus and another lesion in the medial lobe of the right lung. Enlargement of several hilo-mediastinal lymph nodes was noted. Because of dual platelet inhibition, a lymphnode biopsy and pulmonary

wedge biopsy were first delayed but then revealed non-caseating granulomatous tissue without evidence for malignancy. Mycobacteria were not detected, but tissue cultures revealed growth of Nocardia species. Nocardiosis represents an opportunistic infection that may occur in patients on immunosuppressive treatments such as glucocorticoids. It is unknown whether inhibition of IL6 may increase the risk for nocardiosis. A single case report has previously been published on a RA patient treated with glucocorticoids, methotrexate and tocilizumab who presented with nocardia bacteriema. Subsequently, treatment with oral amoxicillin-clavulanic acid was established and continued for 12 months because of an allergic reaction to trimethoprim-sulfamethoxazole, the standard treatment for nocardiosis. Glucocorticoids were successfully tapered and stopped. Clinical signs and symptoms of GCA did not reoccur and CRP and ESR remained normal for over 2 years. It is disputable whether we initially missed nocardiosis as a vasculitic mimic or whether nocardiosis occurred in this patient as a complication of GCA therapy.

Case 4

We want to make you sweat again

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We report the case of a 41-year-old man who presented to our outpatient clinic to investigate a disabling acquired anhidrosis compromising sports practice for 4 years associated with cutaneous xerosis, morning xerostomia, and moderate xerophthalmy. The patient reported chronic swelling of the submandibular glands and heavy night sweats without fever or pruritus. He complained of exertional dyspnea with a tendency to worsen. The clinical examination showed diffuse cutaneous xerosis, erythema of the face and symmetrical painless parotids swelling. There was no lymphadenopathy or synovitis. The neurological status was normal. Blood tests showed elevated ESR (64 mm/h), high ANA titer (1:5120), anti-SSA and anti-SSB positivity. Rheumatoid factor was elevated as IgG levels (polyclonal pattern). Anti-CCP and anti-dsDNA were negative. C3c and C4 levels were in the normal range. Urine analysis showed a 2g/l proteinuria without tubular acidosis or hematuria. Schirmer's test was at the lower limit of the normal range, and the whole unstimulated salivary flow was not reduced. A chest CT scan revealed interstitial damages compatible with lymphoid interstitial pneumonia, consisting of cysts and rare ground-glass areas. Head and neck MRI showed bilateral and symmetrical sublingual, submandibular and parotid hypertrophy, with multiple cysts and canalicular dilation (Rubin and Holt stage 3), but no lymphoma. We made the diagnosis of primary Sjögren's syndrome, according to ACR-EULAR 2016 criteria, with mild dryness symptoms but disabling acquired anhidrosis, pulmonary, glandular, renal and systemic involvement. The patient was first treated with azathioprine, which was not tolerated and then leflunomide, which showed no efficacy. After a multidisciplinary discussion, the patient was treated with rituximab. Since the second cycle of rituximab, the patient described an overall improvement in symptomatology. He started to sweat again on the armpits, abdomen and calves, allowing him to practice sports again. Clinically, we observed a reduction of parotids swelling and resolution of dyspnea. Biologically, we noticed decreased ESR, rheumatoid factor activity and IgG levels. After 18 months under rituximab, the evolution is still favourable, and the treatment is continued. In conclusion, we report a case of Sjögren's syndrome with acquired anhidrosis, successfully treated with rituximab after 18 months of follow-up.

Case 5

Chronic enterovirus infection and myo-fasciitis as a complication of rituximab therapy. A case report.

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Introduction: Humoral deficiency is a significant risk factor that can promote severe acute and chronic enteroviral infections. Rituximab-induced B cell depletion and hypogammaglobulinemia could fail to restrict viral infection and induce high viral load with severe manifestations.

Case report: We report the case of a 27-year-old man with progressive symmetrical polyarthralgias/polymyalgias, chronic diarrhea and constitutional symptoms including fever (39°C). This patient have multiple sclerosis treated with Rituximab since 2017. In 2021, the patient developed a meningitis of undetermined origin. Clinically, the patient presents with peripheral painful tissue swelling as well as abdominal tenderness. Apart from a discrete elevation of the inflammatory syndrome (CRP 32mg/l, VS 2mm/h), the initial biological exploration did not reveal any disturbance of the internal organs. Muscle enzymes did not show any clear disturbance. The complementary investigation of the inflammatory syndrome did not reveal any autoantibodies (FAN, DOT connectivitis, DOT myositis, ANCA), any infectious focus (blood culture, urine culture including search for C. trachomatis and N. gonorrhea, HIV, EBV, CMV, Syphilis, T. whipplei, Lyme) or a neoplastic/vasculitis etiology (PET/CT). MRI of the lower limbs, abdominal and spine revealed a diffuse myo-fasciitis involving mainly the M. gastrocnemius, abdominal and paravertebral musculature. The muscle biopsy (M. gastrocnemius lateralis) had a histological pattern compatible with a vasculopathy, affecting small and medium caliber vessels, of lymphocytic vasculitis type speaking rather in favor of a secondary/reactionary process rather than a primary myopathy/myositis. The specific search for enterovirus in the blood came back positive (enterovirus positive 333000 copies/ml), pan-enterovirus positive 68000 copies/ml). The additional biological analysis shows a hypogammaglobulinemia of IgM, IgA, IgG and subclass known under Rituximab (IgG 3.62g/l, IgG1 1.97g/l, IgG2 1.21g/l. The CSF obtained in 2021 is unfortunately no longer available. The administration of intravenous immunoglobulins (IVg) allowed a clear improvement of the symptomatology as well as of the biological parameters including a normalization of the viral load.

Conclusion: Enteroviral chronic infection with high viral load is a rare complication of rituximab therapy. It can present with myofasciitis. Intravenous immunoglobulin may be a promising therapy.

Case 6

Increased FGF23 and new insufficiency fractures at Burosumab discontinuation in X-linked hypophosphatemia

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Introduction: X-linked hypophosphatemia (XLH), is an inherited lifelong disorder causing chronic hypophosphatemia. XLH lead to over-expression of fibroblast growth factor 23 (FGF23), a circulating hormone with two direct consequences: inhibition of renal phosphate reabsorption and inhibition of 1,25 vitamin D production. In adults, chronic hypophosphatemia causes bone

pain, pseudofractures or fractures. Historically, treatment relied on oral phosphate supplementation and active vitamin D. Since 2018, Burosumab, a monoclonal antibody that binds and inhibits FGF23 activity, has been approved for the treatment of XLH in adults and children. There are insufficient data about the duration of the treatment and no information about clinical, biological or radiological consequences of discontinuation of Burosumab.

Case description: We present a 36-year-old young woman with XLH successfully treated with Burosumab for healing of a threating fracture. The interruption of Burosumab 10 months later, lead to the recurrence of bone pain due to 2 new fractures. Biologically, we assisted to the recurrence of low serum phosphate and 1,25OH vitamin D concentrations, probably related to increased serum FGF23 concentration.

Discussion: Increased serum FGF23 concentration after Burosumab interruption coincided with rapid bone fractures apparition, suggesting a possible FGF23 accumulation after Burosumab treatment interruption with a sort of rebound effect on bone metabolism.

Conclusion: Once initiated, is more judicious to not discontinue Burosumab therapy due to lack of data about consequences and management of interruption of the treatment. Additional evidence is needed to rule on the matter of a possible clinical, biological and radiological rebound effect of Burosumab discontinuation.

HEALTH PROFESSIONALS IN RHEUMATOLOGY (HPR): POSTERS

HPR 1

Rheumatology Transition for Young People in Switzerland – the HEROES Study Methodology

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Background: For up to 50% of children with rheuma, which is a rare pediatric disease, medical care does not end when they reach adulthood and need ongoing medical care throughout their adult lives. A study assessing current transitional care (TC) practice in all 10 pediatric Swiss rheumatology clinics and their adult counterpart showed that the clinics had implemented the standards for good TC only partly. All study sites decided to adapt their TC practice based on the standards for good TC and stakeholder input related to effective TC. The overall aim of the current HEROES-study is to develop, implement and evaluate a TC program for adolescents and young adults (AYA) with a rheumatic disease moving from pediatric to adult settings in Switzerland.

Methods: To ensure a successful and sustainable TC program, this study is based on principle of implementation science. Overall, a hybrid-effectiveness implementation type 2 design is being used. A mixed-methods, participatory partnership approach is used. Intervention development will be based on a taxonomy of O'Cathain which consists of a 7-step (conception, planning, designing, creating, refining, documenting and planning for future evaluation) approach including 18 actions to develop an intervention.

Results: The following implementation outcomes will be assessed by interviews and questionnaires: acceptability, feasibility, appropriateness of the intervention, adoption, fidelity and penetration, and sustainability. Effectiveness outcomes will be assessed at the AYA, parent, healthcare professionals, and healthcare setting/system levels and include quality-of-life, adherence, trust in the healthcare team, satisfaction with TC, and work satisfaction. Economic outcomes will be measured at the AYA, parent, and healthcare setting/system level and will include unplanned healthcare provider visits and absences from work.

Conclusions: The HEROES study will enhance the successful development and long-term implementation of a TC program for AYAs with a rheumatic disease moving from pediatric to adult settings in Switzerland, which will lead to improved patient outcomes. Although the HEROES study focusses on rheumatology, the methods used as well as the results generated can be adopted for other chronic illnesses.

HPR 2

Relationship between person-reported and Observed Quality of Occupational Performance in Activities of Daily Living among Persons with Chronic Pain. A cross-sectional, registry-based study.

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Introduction: Persons with chronic pain are limited in their occupational performance and activities of daily living (ADL). In occupational therapy, both person-reported and observation-based assessments are used to evaluate occupational performance. This study aimed to evaluate if there is a statistically significant and/or strong relationship between person-reported quality of and satisfaction with and the observed quality of ADL motor and ADL process task performance of persons with chronic pain.

Method: The study used a cross-sectional design. Data were collected prospectively in a registry and extracted for this study. The analysis included 143 participants diagnosed with a chronic musculoskeletal pain syndrome. The person-reported quality of and satisfaction with occupational performance was evaluated with the Canadian Occupational Performance Measure (COPM). The Assessment of Motor and Process Skills (AMPS) is a measurement to assess the observed quality of ADL motor and process task performance.

Results: The correlation between the observed quality of ADL motor and person-reported quality of performance was significant but weak. Neither there were significant correlations between the observed quality of ADL motor performance and person-reported satisfaction with performance nor between observed ADL process performance and self-rated quality of and satisfaction with performance.

Conclusion: Observation-based and self-rated assessments seem to provide different but complementary information. Thus, it is recommended to use both self-rated and observational assessments to evaluate the occupational performance of persons with chronic pain.

HPR 3

Das paraspinale Kompartmentsyndrom als seltene Ursache akuter postoperativer Rückenschmerzen

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Ein 77-jähriger Patient, nach einer Whipple-Operation viszeralchirurgisch hospitalisiert, wird uns aufgrund von Rückenschmerzen vorgestellt. Er berichtet von Schmerzen im Bereich der oberen LWS linksseitig, insgesamt seit der Operation (13 Tage zuvor) bestehend und mit zusätzlicher Ausstrahlung in die linke Oberschenkelvorderseite. Klinisch liessen sich die Schmerzen mit einer ausgeprägten Schwellung der paraspinalen Muskulatur linksseitig, "bretthart" imponierend, korrelieren mit begleitender Hypästhesie der Haut direkt über dem schmerzhaften Areal. Zudem war die LWS-Flexion schmerzhaft zu 2/3 eingeschränkt. In anderer Indikation wurde wenige Tage nach der Operation eine CT Abdomen durchgeführt, wobei sich retrospektiv bereits eine deutliche Grössendifferenz der paraspinalen Muskulatur auf Höhe der oberen LWS zeigte. MR-tomographisch liess sich schliesslich die schwere Myopathie der autochthonen Rückenmuskulatur linksseitig mit ausgedehntem Ödem, kräftiger KM-Anreicherung und mehreren Nekrosen nachweisen. Insgesamt war der Befund im Vergleich zur CT-Voruntersuchung wenige Tage postoperativ bereits rückläufig. Korrelierend dazu fiel die (postoperativ bis auf 7535 IU/L erhöhte) CK aktuell normwertig aus. Aufgrund des strengen zeitlichen Zusammenhangs mit der Operation bei mehrstündiger Lagerung auf dem Rücken und leicht zur linken Seite abgekippt, schien ein Lagerungsschaden wahrscheinlich. In Anbetracht aller Befunde liess sich schliesslich nach Literaturdurchsicht ein paraspinales Kompartmentsyndrom vermuten. Passend hierzu ist der plötzliche postoperative Beginn, die "brettharte" Beschaffenheit der Muskulatur mit umschriebener massiver Druckdolenz, die streng über dem schmerzhaften Bereich lokalisierte Hypästhesie, die CK-Erhöhung auf >2000IU/L und der typische T2-hyperintense MRI-Befund. Weiter passend ist die schmerzhafte Flexion bei schmerzfreier Extension und

die im Verlauf auftretende radikuläre / pseudoradikuläre Ausstrahlung in die untere Extremität. Es handelt sich um eine sehr seltene (oder unterdiagnostizierte) Ursache von akuten postoperativen, oder in Verbindung mit bestimmten Sportarten (z.B. Gewichtheben) / direkten Traumata auftretenden Rückenschmerzen mit bisher 37 Fallbeschreibungen weltweit. Die Therapie richtet sich primär nach dem Verlauf. Faszienspaltungen können analog zum Kompartmentsyndrom an den Extremitäten eingesetzt werden. Aufgrund des guten Spontanverlaufs wurde ein operativer Eingriff in unserem Fall aber nicht notwendig.

HPR 4

Advanced practice nurse-led gout consultations

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Gout is a painful condition often attributed to poor lifestyle choices, but it can also be triggered by genetics, kidney failure, and medication. During an attack, the affected joints become swollen and inflamed causing extreme pain due to a high level of uric acid in the blood. Men are more likely to suffer from gout, with 80% of sufferers, and the first attack typically occurs between the ages of 55 and 60. Due to the protective effects of estrogen, women rarely develop gout before menopause.

The objective of gout treatment is to reduce the level of uric acid in the blood. This can be done pharmacologically with long-term therapy and attack prophylaxis, or non-pharmacologically with a focus on diet, reduced alcohol consumption, physical activity, and weight management. Despite the well-known therapy of the disease, which can be simply integrated into a patient's daily routine, studies show that only 30% of gout patients receive the necessary therapies.

Literature shows that continuous care from Advance Practice nurses (APNs) has significantly reduced uric acid levels in gout patients as a result of the support patients receive in disease self-management, health-literacy and guide them on the importance of medication adherence and lifestyle changes.

Therefore, to address the undersupply of care for gout patients, the University Hospital of Bern introduced a nurse-led consultation by an APN in late April 2023. This new service is a step towards improving the care of gout patients in Switzerland.

The consultation aims to strengthen patients' personal health literacy and self-management of the disease by providing information on all aspects of the disease including medication, nutrition, and lifestyle. Each consultation follows a structured approach, beginning with a blood sample and a consultation with the APN, followed by medication prescription and joint assessment by the gout specialist. If needed a referral to a nutritionist, occupational therapist, and physiotherapist happens.

Although this consultation has just started, it is expected to significantly enhance the self-management, health literacy, and adherence of gout patients to live symptom-free life and discontinue their medication in the future.

HPR 5

Pain in participants of a Swiss fall prevention study

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Background: For a fall prevention study, we recruited 405 people aged 65 years or older who did either fall in the previous 12 months or expressed fear of falling. The primary objective of the study was to assess the effectiveness of three home-exercise programs designed to reduce fall risk. Exercise, especially resistance exercises, was shown to have a positive effect on pain. As pain has an influence on well-being, we wanted to evaluate in this secondary analysis whether there was a decrease in pain and an increase in well-being over the study period. Other aims were to document the prevalence of pain and the average pain intensity among the participants.

Methods: Secondary analyses of a randomized controlled falls prevention trial in four regions in the French and German-speaking parts of Switzerland. Pain was not a primary outcome and was assessed with one question about pain intensity rated on a visual analogue scale from 0 to 100 at baseline, six and twelve months, and one question about pain affecting well-being from the OPQOL-35 questionnaire ("pain affects my well-being, strongly agree to strongly disagree"), assessed at baseline, six and twelve months.

Results: At baseline, 76% of the participants reported pain. Those with pain reported an average of 50.0 points (standard deviation 18.8) on a scale from 0 to 100. Well-being was affected in 58% of the participants. If we only analyse participants who had data at baseline and at six months, 58% reported pain affecting well-being at baseline and 59% at six months. Of those with affected well-being at baseline, 28% improved and reported that pain did not affect well-being at six months, and 42% of those without affected well-being reported being affected by pain at six months. On average, pain intensity did not decrease from baseline to six or to twelve months. Pain intensity was not a predictor for the number of falls.

Conclusion: First, a substantial percentage of individuals at high risk of falling experience pain that significantly impacts their overall well-being. Among those with pain, pain intensity is quite high (50 points on a 0 to 100 scale). Second, the balance and resistance exercises targeted to reduce fall risk did not influence pain, and there was no difference between the three home-based exercise programmes. Further research should evaluate whether additional pain-related patient education in falls-prevention programmes could improve pain-related outcomes.

HPR 6

Erste Subgruppenanalyse der RZA- und AAV-Patienten aus dem Vaskulitis-Register GeVas

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Einleitung: Vaskulitiden sind seltene Erkrankungen, es bestehen viele Evidenzlücken u.a. bezüglich der bestmöglichen Therapien. Viele Studien sind retrospektiv und monozentrisch mit relativ kleinen Patientenzahlen. Im Gemeinsamen Vaskulitis-Registers im deutschsprachigen Raum (GeVas) werden Patienten erfasst, bei denen eine Vaskulitis neu diagnostiziert oder bei denen die Therapie aufgrund eines Rezidivs geändert wurde. GeVas ermöglicht eine prospektive, multizentrische, webbasierte Dokumentation von Organmanifestationen, Therapieschemata und Langzeitergebnissen bei einer großen Kohorte mit verschiedenen Vaskulitiden. Wir berichten über die

Patienten mit Riesenzellarteriitis (RZA) und ANCA-assoziierter Vaskulitis (AAV).

Ergebnis: Seit Juni 2019 rekrutieren 18 Zentren in D (Stand Oktober 2022 >500 Patienten). Den größten Anteil stellen die AAV mit 266 sowie die RZA mit 191 Patienten. Jeweils ca. 2/3 wurden bei Erstdiagnose und 1/3 bei Rezidiv eingeschlossen. Die Geschlechtsverteilung war wie folgt: RZA-Kohorte 64 % weiblich und 36 % männlich, AAV-Kohorte je ca. 50%. Das mediane Alter war 59 Jahre (51-70a) bei den AAV-Patienten, die RZA-Patienten waren mit 73 Jahren im Schnitt erwartungsgemäss älter (52-91a). Bei den AAV hatten 61% eine GPA, 25% eine MPA, 13% eine EGPA und 1% eine renal limited AAV. Am häufigsten wurden bei RZA-Patienten kraniale Symptome, eine Augenbeteiligung und eine Beteiligung des kardiovaskulären Systems (= Aortitis) festgestellt. In aller Regel erhielten AAV und RZA Patienten Glucokortikoide, eine Induktionstherapie bei AAV wurden bei 45 % mit RTX und bei 42% mit Cyc durchgeführt. 48 % der RZA-Patienten erhielten TCZ als zusätzliche immunsuppressive Therapie, 20 % MTX und 16 % Cyc.

Zusammenfassung: Im Juni 2019 wurde das prospektive multizentrische Vaskulitis-Register GeVas etabliert. Nach 3,5 Jahren Follow-up-Dokumentation wurden die ersten Langzeitergebnisse ausgewertet und interpretiert. Die Daten u.a. zu Krankheitsmanifestation und Therapieschemata geben wichtige Einblicke in die Behandlung von Vaskulitis Patienten. Für die Schweiz besteht bereits die Möglichkeit zur Dokumentation von RZA-Patienten im SCQM-Register (www.SCQM.ch), ein ANCA-Register ist in Kooperation mit der Vasculitis Association of Switzerland im Aufbau (www.VASAS.ch). Eine aktive Teilnahme vieler Kliniken und Praxen ist sehr erwünscht. Ein Vergleich der Daten des GeVas Registers und der Schweizer Register ist geplant.

INDUSTRY: POSTERS

IP 1

Achievement of low disease activity over 52 weeks in patients with active axial spondyloarthritis on bimekizumab treatment: Results from the phase 3 studies BE MOBILE 1 and BE MOBILE 2

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Background: The recommended treatment target for axial spondyloarthritis (axSpA) is remission/low disease activity (LDA; ASDAS <2.1) by ASDAS levels. [1]

Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F and IL-17A. We report LDA achievement to Week (Wk)52 in the BE MOBILE 1 and 2 phase 3 studies of BKZ in non-radiographic (nr-) and radiographic (r-)axSpA (i.e. ankylosing spondylitis). [2, 3]

Methods: BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) comprised 16-wk placebo (PBO)-controlled and 36-wk maintenance periods.3 BE MOBILE 1 (nr-axSpA) patients (pts) met ASAS classification criteria and had objective inflammation (by MRI and/or elevated CRP); BE MOBILE 2 (r-axSpA) pts fulfilled modified New York and ASAS criteria. All pts had active disease (BASDAI≥4, spinal pain≥4 [BASDAI item 2]) at baseline. Pts were randomised to subcutaneous BKZ 160mg every 4 wks (Q4W) or PBO. PBO-randomised pts switched to BKZ Q4W from Wk16 (PBO/BKZ).3 Pts (%) achieving LDA defined by ASDAS <2.1 and/or BASDAI <4 to Wk52 are presented (non-responder imputation).

Results: 254 nr-axSpA pts (BKZ:128; PBO:126) and 332 r-axSpA pts (BKZ:221; PBO:111) were randomised. Most had high/very high disease activity (ASDAS≥2.1) at baseline (nr-axSpA: BKZ:99.2%, PBO:97.6%; r-axSpA: BKZ:98.6%, PBO:100%). At Wk16, greater proportions of BKZ v PBO pts with nr-axSpA achieved ASDAS <2.1 (46.1% v 19.8%), BASDAI <4 (52.3% v 31.7%), and both (43.8% v 19.0%). Results were similar in r-axSpA pts for ASDAS <2.1 (42.1% v 17.1%), BASDAI <4 (55.7% v 41.4%), and both (41.6% v 17.1%). Separation from PBO was seen from Wk2 for ASDAS <2.1 and both ASDAS <2.1 and BASDAI <4. By Wk52, LDA achievement in continuous BKZ and PBO/BKZ pts was similar for ASDAS <2.1 (53.9% v 47.6%), BASDAI <4 (60.2% v 54.0%) and both (49.2% v 45.2%). The same was true for r-axSpA: ASDAS <2.1 (50.2% v 61.3%); BASDAI <4 (65.6% v 68.5%); both (49.8% v 58.6%). BASDAI <4 response was consistently higher than ASDAS <2.1 in both arms.

Conclusions: BKZ led to rapid achievement of ASDAS <2.1, BASDAI <4, and both to Wk16 vs PBO; improvements continued to Wk52. Most pts with ASDAS <2.1 achieved BASDAI <4, suggesting ASDAS <2.1 is a more stringent criterion for LDA, relevant when considering BKZ in a potential treat-to-target approach for axSpA.

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IP 2

Resolution of enthesitis and peripheral arthritis with bimekizumab in patients with axial spondyloarthritis: Week 52 results from the BE MOBILE 1 and BE MOBILE 2 Phase 3 studies

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Introduction: History of enthesitis or peripheral arthritis has been reported in >30% of axial spondyloarthritis (axSpA) patients (pts). Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F and IL-17A, has shown efficacy in non-radiographic (nr-)axSpA (BE MOBILE 1) and radiographic axSpA (r-axSpA; BE MOBILE 2) pts. We evaluate impact of BKZ on axSpA peripheral manifestations to Week (Wk)52.

Methods: BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) pts were randomised to subcutaneous BKZ 160mg every 4wks (Q4W) or placebo (PBO) to Wk16. From Wk16, all pts received BKZ Q4W.

In pts with enthesitis (MASES>0), >0 swollen joint (SJC>0), or >0 tender joint (TJC>0) at baseline (BL), we report mean change from BL (CfB). Pt proportions achieving enthesitis resolution (MASES = 0 in pts with BL MASES>0) and peripheral arthritis (SJC = 0 in pts with BL SJC>0) are reported.

Results: At BL, 73.2% nr-axSpA (BKZ:94/128, PBO:92/126) and 59.9% r-axSpA pts (BKZ:132/221, PBO:67/111) had enthesitis; peripheral arthritis (SJC>0) was present in 34.6% (BKZ:45/128, PBO:43/126) and 19.9% (BKZ:44/221, PBO:22/111) nr-axSpA and r-axSpA pts. BL MASES (nr-axSpA: BKZ:4.8, PBO:4.9; r-axSpA: BKZ:4.2, PBO:4.4), SJC (nr-axSpA: BKZ:4.2, PBO:3.8; r-axSpA: BKZ:4.7, PBO:3.9) and TJC (nr-axSpA: BKZ:6.0, PBO:6.3; r-axSpA: BKZ:5.3, PBO:5.4) were similar between treatment arms.

Greater CfB in MASES was achieved with BKZ vs PBO at Wk16; improvements continued to Wk52 in BKZ and PBO/BKZ pts (nr-axSpA: BKZ:-3.6, PBO/BKZ:-2.9; r-axSpA: BKZ:-2.9, PBO/BKZ:-3.2). >50% BKZ pts achieved complete enthesitis resolution at Wk16 vs <33% of PBO pts; by Wk52, PBO/BKZ pt (nr-axSpA:44.6%; r-axSpA:46.3%) responses approached those of BKZ pts (nr-axSpA:54.3%; r-axSpA:50.8%).

At Wk16, greater CfB in SJC and TJC was achieved in BKZ vs PBO-randomised nr-axSpA pts. Improvements largely continued to Wk52 in both arms (SJC: nr-axSpA: BKZ:-2.5, PBO/BKZ:-2.9; r-axSpA: BKZ:-4.2, PBO/BKZ:-3.6; TJC: nr-axSpA: BKZ:-4.0, PBO/BKZ:-3.5; r-axSpA: BKZ:-4.0, PBO/BKZ:-4.5). >57% BKZ vs >36% PBO-randomised pts achieved peripheral arthritis resolution at Wk16; by Wk52, proportions were similar among BKZ (nr-axSpA:62.2%; r-axSpA:72.7%) and PBO/BKZ pts (nr-axSpA:65.1%; r-axSpA:81.8%).

Conclusions: BKZ resulted in sustained improvements in peripheral manifestations across the axSpA spectrum; large proportions of pts achieved enthesitis and peripheral arthritis resolution by Wk52.

IP 3

Achievement of increasingly stringent clinical disease control criteria was associated with greater improvements in physical function, pain and fatigue in patients with active psoriatic arthritis: 52-Week results from BE OPTIMAL, a phase 3 randomised, placebo-controlled study

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Introduction: Psoriatic arthritis (PsA) joint/skin manifestations place substantial burden on patient (pt) quality of life. [1] Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.

We examine associations between achieving clinical disease control criteria and patient-reported measures of physical function, pain and fatigue in pts with PsA.

Methods: BE OPTIMAL (NCT03895203) comprised a 16-wk double-blind placebo (PBO)-controlled period and 36-wk treatment-blind period. Pts were ≥18 years, biologic disease-modifying antirheumatic drug naïve, with adult-onset, active PsA, ≥3 tender and ≥3 swollen joints. Pts were randomised 3:2:1, BKZ 160 mg every 4 weeks (Q4W):PBO:adalimumab 40 mg Q2W. From Wk16, PBO pts received BKZ Q4W. In this analysis, all pts who reached specified disease control criteria (ACR: <ACR20, ACR20– <ACR50, ACR50– <ACR70, ACR70; ACR50 and Psoriasis Area and Severity Index 100 [ACR50+PASI100]: non-responder/responder; Disease Activity in PsA [DAPSA]: high/moderate/low disease activity or remission [HDA, MoDA and LDA/REM]; Minimal Disease Activity [MDA]: non-MDA/MDA) at Wk52 were pooled across treatments. Associations between achieving these criteria and improvements in patient-reported physical function and symptom measures were assessed (Health Assessment Questionnaire Disability Index [HAQ-DI], Pt's Assessment of Arthritis Pain Visual Analog Scale [Pain VAS], Functional Assessment of Chronic Illness Therapy-Fatigue subscale [FACIT-Fatigue]). Some aspects of the disease control criteria relate to aspects of HAQ-DI and PtAAP. Data are observed case.

Results: 761/852 (89.3%) pts completed Wk52. Baseline mean (SD) HAQ-DI (0[best]–3[worst]), Pain VAS (0[best]–100[worst]) and FACIT-Fatigue (0[worst]–52[best]): 0.85 (0.59), 55.2 (23.9) and 37.0 (9.7). Pts achieving higher ACR responses demonstrated greater mean (95% CI) improvements from baseline in HAQ-DI (<ACR20: 0.0 [–0.1, 0.1]; ACR70: –0.6 [–0.7,

–0.6]), Pain VAS (<ACR20: –3.8 [–7.7, 0.1]; ACR70: –49.6 [–52.2, –46.9]) and FACIT-Fatigue (<ACR20: 0.2 [0.0, 0.3]; ACR70: 1.0 [0.9, 1.1]). Similar improvements were seen with achievement of ACR50+PASI100, increasing DAPSA thresholds and MDA.

Conclusions: Pts with PsA achieving stringent disease control criteria reported greater improvements in physical function, pain and fatigue at Wk 52.

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IP 4

Sustained efficacy and safety of bimekizumab in patients with active psoriatic arthritis and prior inadequate response to tumour necrosis factor inhibitors: Results from the phase 3 BE COMPLETE study and its open-label extension up to 1 year

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Background: Bimekizumab (BKZ) has demonstrated efficacy to 16 weeks (wks) vs placebo (PBO), tolerability in psoriatic arthritis (PsA) patients (pts) and efficacy to 52 wks in biologic-naïve PsA pts.1–3

We assess BKZ efficacy and safety to 52 wks in PsA pts with prior inadequate response to TNFi.

Methods: BE COMPLETE (NCT03896581) included a 16-wk double-blind, PBO-controlled period. Wk16 completers were eligible for BE VITAL entry (NCT04009499; open-label extension). Data here include pts randomised in BE COMPLETE only: 2:1 BKZ 160mg Q4W:PBO. At Wk16, PBO pts switched to BKZ (PBO/BKZ). Efficacy data are reported using non-responder/multiple imputation (binary/continuous). Treatment-emergent adverse events (TEAEs) are reported to Wk52 for pts who received ≥1 BKZ dose, including PBO/BKZ switchers.

Results: 347/400 (86.8%) pts completed Wk52. At Wk16 43.4% BKZ and 6.8% PBO pts achieved ACR50; at Wk52 51.7% BKZ and 40.6% PBO/BKZ pts achieved ACR50. In pts with baseline (BL) psoriasis (≥3% body surface area), 58.8% BKZ and 4.5% PBO pts achieved PASI100 (complete skin clearance) at Wk16; at Wk52 65.9% BKZ and 60.2% PBO/BKZ pts achieved PASI100. At Wk16 44.2% BKZ and 6.0% PBO pts achieved minimal disease activity (MDA); at Wk52 47.2% BKZ and 33.1% PBO/BKZ

pts achieved MDA. Reductions from BL in HAQ-DI scores (mean [SE]) were sustained from Wk16 (–0.38 [0.03] BKZ; –0.07 [0.04] PBO) to Wk52 (–0.39 [0.03] BKZ; –0.35 [0.05] PBO/BKZ). In pts with mNAPSI >0 at BL, mNAPSI resolution rates increased from Wk16 (45.9% BKZ; 14.5% PBO) to Wk52 (67.3% BKZ; 61.4% PBO/BKZ).

To Wk52, 243/388 (62.6%) BKZ-treated pts had ≥1 TEAE (126.0/100 pt-years [PY]); 23 (5.9%) reported a serious TEAE (7.0/100PY). Two (0.7%) BKZ-treated pts reported malignancies excluding non-melanomic skin cancers (0.77/100PY). 25 (6.4%) BKZ-treated pts reported Candida infections (7.7/100PY); all mild/moderate; none systemic. Two oral candidiasis cases led to study discontinuation. There was one death (sudden death; pt with cardiac history); two adjudicated major adverse cardiac events; no definite/probable adjudicated inflammatory bowel disease.

Conclusions: BKZ demonstrated sustained efficacy from Wk16–52 in PsA pts with TNFi-IR; safety profile consistent with previous reports.1–3

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IP 5

Safety Profile of Upadacitinib up to 6.5 Years of Exposure in Patients with Rheumatoid Arthritis

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Background: Upadacitinib (UPA) has demonstrated safety and efficacy in patients (pts) with moderate-to-severe active RA in the phase 3 SELECT clinical program. Here we describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA from the SELECT clinical program.

Methods: Pooled safety data were analyzed from 6 randomized controlled trials evaluating UPA in RA. TEAEs and AESIs were summarized for these groups: pooled UPA 15 mg QD (UPA15, 6 trials), MTX (1 trial), and adalimumab (ADA) 40 mg EOW (1 trial). TEAEs were defined as AEs with an onset after the first dose and ≤ 30 days (UPA and MTX) or ≤ 70 days (ADA) after the last dose and reported as EAERs per 100 PY (E/100 PY). The standardized mortality ratio (SMR) was estimated for the general population using WHO country-age-gender specific mortality rates through 2016.

Results: 3209 pts received ≥ 1 dose of UPA15 with 10 782.7 PY of exposure. EAERs of AEs, serious AEs (SAEs), and AEs leading to discontinuation on UPA15 were comparable to MTX and ADA. COVID-19 pneumonia was the most common SAE with UPA15 (0.7 E/100 PY). Rates of serious infections were similar UPA15 vs ADA but higher compared with MTX. Herpes zoster (HZ) rates were higher with UPA15 vs MTX and ADA. Most HZ cases

with UPA15 were non-serious (95%) and affected a single dermatome (75%) or unilateral multiple dermatomes (16%); 8% of cases were reported as disseminated and none involved the CNS. CPK elevations were transient and more common with UPA15 vs MTX or ADA. Anemia and neutropenia rates were similar in UPA15 vs ADA. Most hepatic disorders were mild or moderate transaminase elevations. Treatment discontinuation due to these lab events was rare (≤ 0.1 E/100 PY). Similar rates of adjudicated MACE, adjudicated VTE, and malignancy (excl. NMSC) were observed across treatment groups. The NMSC rate was numerically higher with UPA15 vs ADA; no cases occurred with MTX. SMR analysis indicated that the mortality rate among RA pts treated with UPA15 was not higher than what would be expected among the general population (SMR [95% CI]: 0.67 [0.52, 0.86] incl. COVID-19 deaths; 0.41 [0.29, 0.56] excl. COVID-19 deaths).

Conclusions: The integrated safety profile of UPA in pts with RA remained consistent with previous findings, with no new safety risks identified up to 6.5 years of exposure. Similar rates of AESIs were observed for UPA15 and ADA, except for higher rates of HZ, CPK elevations, and NMSC with UPA.

IP 6

Long-term Safety of Upadacitinib in Psoriatic Arthritis, Ankylosing Spondylitis, and Non-radiographic Axial Spondyloarthritis up to 5 Years

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Background: The efficacy and safety of upadacitinib (UPA) has been demonstrated in phase 3 trials for PsA, AS, and nr-axSpA. Here we provide a safety update for UPA across PsA, AS, nr-axSpA, and pooled axSpA from the SELECT program.

Methods: Safety data (cut-off: 15 Aug 2022) from 5 UPA trials in PsA (2), AS (2), and nr-axSpA (1) were compiled. TEAEs (onset on or after first dose and ≤30 days for UPA 15 mg [UPA15], or ≤70 days for adalimumab [ADA], after last dose) were summarized for PsA (pooled UPA15 and ADA [1 study only]), AS (pooled UPA15), nr-axSpA (UPA15), and pooled axSpA (pooled UPA15 from AS and nr-axSpA trials). TEAEs are reported as EAERs (events/100 patient-years [E/100 PY]). Age-gender adjusted standard incidence ratios (SIRs) using the SEER database and standardized mortality ratios (SMRs) were calculated.

Results: A total of 1789 patients (PsA, n = 907; AS, n = 596; nr-axSpA, n = 286) received ≥1 dose of UPA15, totaling ~3690 PY of exposure. Overall AEs and serious AEs were highest in PsA, and numerically higher with UPA15 vs ADA; rates were generally similar between AS and nr-axSpA. AEs leading to discontinuation were generally similar across treatment groups and diseases and were numerically lowest in AS. Rates of malignancy excl. NMSC, MACE, and VTE were similar between UPA15 and ADA in PsA and were generally similar across diseases. In PsA, higher rates of serious infection, herpes zoster (HZ), lymphopenia, and NMSC were observed with UPA15 vs ADA. The SIR (95% CI) for malignancy excl. NMSC with UPA15 was 0.94 (0.54-1.53) in PsA and 0.58 (0.12-1.69) in pooled axSpA; SIRs for AS (1 case) and nr-axSpA (2 cases) were not calculated separately due to low events. In PsA, the SMR (95% CI) with UPA15 was 0.71 (0.40-1.18), and 0.33 (0.13-0.69) with COVID-19 deaths excluded, suggesting no increased risk of death vs the general population. SMRs were not calculated for AS, nr-axSpA, or pooled axSpA due to low events. Data from this analysis

should be interpreted with caution, as it was not enriched for AEs and duration of exposure was more limited for AS and nr-axSpA.

Conclusions: Higher rates of serious infection, HZ, lymphopenia, and NMSC were observed with UPA15 vs ADA in PsA; slightly elevated rates for most of these TEAEs were also observed with UPA15 in PsA vs axSpA. Apart from these differences, UPA15 demonstrated a generally consistent safety profile across disease states, with no new safety signals identified from previous reports.

IP 7

Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response to Conventional Synthetic DMARDs: Results Through 5 Years From the SELECT-NEXT Study

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Background: In the phase 3 SELECT-NEXT study, upadacitinib (UPA) demonstrated efficacy at wk 12 and sustained efficacy up to wk 60 in csDMARD-IR RA patients (pts). Here, we evaluated the efficacy and safety of UPA up to 5 yrs in a LTE of SELECT-NEXT.

Methods: Pts received UPA 15 mg (UPA15) or 30 mg (UPA30) QD or placebo (PBO) for 12 wks, with stable background csDMARDs. PBO pts were switched to UPA15/30 in a pre-specified manner at wk 12. From wk 12, pts were able to enter a blinded LTE for up to 5 yrs, in which all pts received UPA15 or UPA30. The blinded LTE remained until dose switching from UPA30 to UPA15 (earliest switch at wk 168). For pts not meeting CDAI ≤10 at or after wk 24, investigators were instructed to adjust background RA therapies. Efficacy data up to wk 260 are reported as observed (AO) for UPA15/UPA30 pts. TEAEs per 100 PY were summarized over 5 yrs.

Results: Of the 661 pts randomized at BL, 611 (92%) completed wk 12 and entered the 248-wk LTE. In total, 271 (41%) pts discontinued study drug during the LTE due to AEs (16%), withdrawal of consent (10%), loss to follow-up (3%), lack of efficacy (3%), or other reasons (9%). Clinical outcomes continued to improve or were maintained through wk 260, with 51% and 43% of pts achieving CDAI remission and 75% and 66% attaining DAS28(CRP) <2.6 with UPA15 and UPA30, respectively (AO). Over half of pts achieved ACR70 on either UPA dose (AO). Lower efficacy estimates based on NRI were consistent for UPA15/30. Physical function and pain improved similarly with UPA15/30 at wk 260; the mean change from BL was -0.86/-0.78 for HAQ-DI and -44/-44 mm for pain (AO). Pts who switched from PBO to UPA at wk 12 showed similar efficacy as those initiated on UPA (data not shown). Through 5 yrs, TEAEs and AESIs were consistent with previous study-specific analyses. Numerically higher rates of any AE, serious AEs, any infection, serious infections, herpes zoster, NMSC, and neutropenia were observed with UPA30 vs UPA15. While malignancies (excl. NMSC) and MACE were rare, numerically higher rates were also observed with UPA30 vs UPA15.

Conclusions: UPA15/30 therapy with background csDMARDs demonstrated sustained efficacy across multiple RA disease activity measures through the 5-yr study period. The safety profile was consistent with earlier time points and with an integrated phase 3 safety analysis of UPA in RA, although dose-dependent increases in the rates of certain AEs were noted in pts receiving UPA30 vs UPA15.

IP 8

Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response or Intolerance to Biologic DMARDs: Results Through 5 Years From the SELECT-BEYOND Study

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Background: To evaluate the long-term efficacy and safety of upadacitinib (UPA) over 5 yrs among patients (pts) with RA in a long-term extension (LTE) of the SELECT-BEYOND study.

Methods: In SELECT-BEYOND (a double-blind, randomized phase 3 trial), bDMARD-IR pts received UPA 15 mg (UPA15) or 30 mg (UPA30) QD or placebo (PBO) for 12 wks, each with background csDMARD(s). From wk 12 onwards, pts randomized to PBO switched to UPA15 or UPA30 in a prespecified manner. All pts who completed the wk 24 visit could enter an LTE of up to a total of 5 yrs. Pts receiving UPA30 switched to UPA15 (earliest switch at wk 180). Efficacy data up to wk 260 are shown for pts randomized to UPA15/30 and reported as observed (AO); missing data for categorical endpoints were also imputed using NRI. TEAEs per 100 PY were summarized over 5 yrs for UPA15 and UPA30 and shown separately for those who switched from UPA30 to UPA15.

Results: Of the 498 pts randomized, 418 (84%) completed wk 24 and entered the LTE. During the LTE, 197 (40%) pts discontinued study drug due to TEAEs (13%), withdrawal of consent (7%), lack of efficacy (6%), lost to follow-up (4%), or other reasons (11%). Of the pts receiving concomitant corticosteroid or csDMARDs at baseline (BL), approximately 20% and 10%, respectively, discontinued their use during the study. In both UPA groups, pts demonstrated similar clinical improvements over 5 yrs. At wk 260 e.g., 36%/36% and 81%/77% of UPA15/30 pts achieved CDAI remission or LDA, respectively (AO). By wk 260, 88%/68%/51% of pts achieved ACR20/50/70 responses on UPA15 and 88%/67%/46% on UPA30 (AO). Boolean remission was achieved by 28% of pts on UPA15 and 23% on UPA30 (AO). Functional and pain-related outcomes showed similar improvements with UPA15/30: the mean change from BL was -0.6/-0.6 for HAQ-DI and -39/-37 mm for patient's assessment of pain (AO). No apparent loss of benefit was observed with UPA15 in pts who switched from UPA30. Dose-dependent increases in rates of herpes zoster and CPK elevation were observed with UPA30 vs UPA15. Treatment-emergent deaths were comparable between both UPA doses. No new safety issues were identified from the long-term study.

Conclusions: Treatment with either UPA15 or UPA30 continued to be effective in improving clinical and functional outcomes in RA. Notably, at wk 260, over three-quarters of pts attained CDAI LDA. Overall, the safety profile over 5 yrs was consistent with earlier assessments of UPA treatment in this population.

IP 9

Impact of Upadacitinib Versus Abatacept on Individual Disease Outcomes in Pts With Rheumatoid Arthritis and Inadequate Responses to Biologic DMARDS

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Background: The phase 3 SELECT-CHOICE trial of bDMARD-IR RA patients (pts) demonstrated superiority of the JAK inhibitor upadacitinib (UPA) vs abatacept (ABA) in the mean change from baseline (BL) in DAS28(CRP) and in the proportion achieving DAS28(CRP) <2.6 at week (wk) 12, with higher incidence of serious adverse events reported in the UPA treatment group.

Methods: Pts were randomly assigned to UPA 15 mg once daily or ABA, each with background csDMARDs, for 24 wks. For this post hoc analysis, the proportions of pts achieving improvement from BL through wk 24 in ACR core variables (including SJC, TJC, PtGA, PhGA, pain, HAQ-DI, and hsCRP) and Boolean remission criteria were evaluated. Differences in the cumulative distributions of CDAI, DAS28(hsCRP), SDAI, and ACR-n were determined using the Kolmogorov-Smirnov test and are reported AO. For all other variables, NRI was applied for missing data. Nominal P values are provided throughout.

Results: A total of 616 bDMARD-IR pts with moderate to severe RA were randomized (UPA 15 mg, n = 303; ABA, n = 309). BL demographic and disease characteristics were comparable between treatment groups, with a mean disease duration of approximately 12 yrs and mean CDAI of 39.6. At wk 12, more pts receiving UPA vs ABA achieved ≥50% improvements from BL in TJC68, PtGA, and hsCRP, with comparable proportions observed between UPA and ABA for the remaining ACR components. At wk 24, similar proportions of pts receiving UPA and ABA achieved ≥50% improvements in all but the hsCRP component. Overall, 15% and 26% of pts on UPA compared with 6% and 15% on ABA demonstrated ≥50% improvements across all ACR components at wks 12 and 24, respectively. At wks 12 and 24, Boolean remission was achieved by 6% and 14% of pts on UPA vs 2% and 10% of pts on ABA, respectively; the proportion of pts in both treatment groups achieving the individual Boolean components were also reported. While comparable at BL, cumulative distributions of CDAI, SDAI, DAS28(hsCRP), and ACR-n were improved on UPA vs ABA at wk 12 (all nominal P <0.05); differences persisted for most measures at wk 24.

Conclusions: In this post hoc analysis of bDMARD-IR RA pts, improvements in components of disease measures were reported for both UPA and ABA through 24 weeks, with numeric differences noted for several components. Nominally higher attainment of Boolean remission and its components were observed for UPA over ABA.

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