SMW
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Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift
An open access, online journal • www.smw.ch

Supplementum 261
ad Swiss Med Wkly
2022;152
August 31, 2022

Abstracts of the joint annual meeting of the Swiss Society of Rheumatology and the Swiss Society of Physical Medicine and Rehabilitation

Interlaken (Switzerland), September 8/9, 2022

EMH Media
SCHWEIZERISCHER ÄRZTEVERLAG
EDITIONS MEDICALES SUISSES

SWISS SOCIETY OF RHEUMATOLOGY

SWISS SOCIETY OF PHYSICAL MEDICINE AND REHABILITATION

JOINT ANNUAL CONGRESS 2022

INTERLAKEN, SEPTEMBER 8–9, 2022

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BEST ABSTRACT PRESENTATION

OP 1

Increased humoral immune response after vaccination with mRNA-1273 vs BNT162b2 in patients with inflammatory rheumatic diseases

Raptis CE[1], Berger CT[2,3], Andrey DO[4], Polysopoulos C[1], Ciurea A[5], Lescuyer P[4], Maletic T[1], Riek M[1], Scherer A[1], von Loga I[1], Safford J[6], Lauper K[7], Möller B[8], Vuilleumier N[4], Finckh A[7], Rubbert-Roth A[9]

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Patients with inflammatory rheumatic diseases (IRD) have an increased risk for a worse COVID-19 outcome, and impaired immune responses following mRNA COVID-19 vaccines have been observed. In this prospective observational study, we compared the anti-S1 response following vaccination with BNT162b2 and mRNA-1273 in a large cohort of IRD patients and assessed the effect of different immunomodulatory treatments.

Patients from SCQM, the Swiss IRD cohort, who assented to an mRNA COVID-19 vaccine were recruited into the study between 3/2021-9/2021. Participants answered the study questionnaire via the mySCQM patient app and provided self-collected capillary blood samples at baseline, 4, 12, and 24 weeks post second vaccine dose. Samples were tested for IgG antibodies against the S1 domain of the SARS-CoV-2 spike protein using the EUROIMMUN ELISA. We examined differences in antibody titres depending on the vaccine and treatment received, while adjusting for age and history of SARS-CoV-2 infection, by applying mixed effects continuous outcome logistic regression models at each timepoint.

Eligible samples were obtained from 564 IRD patients (mean age 53 y (s.d. 12 y), 66% female) with 36% RA, 37%, axSpA, 21% PsA, and 6% UA (undifferentiated arthritis), on no medication (no DMARD & no steroids 15%), csDMARD (9%), TNFi (48%), IL-6/17/23i (14%), JAKi (6%), rituximab (4%), abatacept (3%), and PDE4i (1%) in mono/combination therapy at baseline. 10% of patients had a past SARS-CoV-2 infection, 54% received BNT162b2, 46% mRNA-1273. Independently of the disease, treatment, and history of SARS-CoV-2 infection, the odds of having higher anti-S1 titres at 4, 12, and 24 weeks post second vaccine dose were, respectively, 3.3, 3.9, and 3.8 times higher with mRNA-1273 compared to BNT162b2 for the average-aged patient of this population ($p < 0.0001$). Moreover, with every year of age, the odds of higher anti-S1 levels increased by 3% to 5% following mRNA-1273 vs BNT162b2 vaccination ($p < 0.05$), indicating an additional benefit for elderly IRD patients. Among monotherapies, rituximab, abatacept, JAKi, and TNFi had the highest odds of reduced anti-S1 responses compared to no medication. Patients on specific combination therapies showed significantly reduced antibody responses compared to respective monotherapies.

Our results suggest that in IRD patients, vaccination with mRNA-1273 vs BNT162b2 results in higher anti-S1 antibody titres, and has an additional benefit in elderly patients.

OP 2

Comparison of anti-fracture effectiveness of denosumab versus bisphosphonates in a registry-based, real-world cohort study

Everts-Graber J[1,2], Bonel H[3,4,5], Lehmann D[6], Gahl B[7], Häuselmann HJ[8], Studer U[1], Ziswiler HR[1], Reichenbach S[2,9], Lehmann T[1]

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Background: Head-to-head studies showed greater efficacy of denosumab versus bisphosphonates in improving bone mineral density, but clinical studies designed to compare the anti-fracture efficacy of denosumab with BPs are lacking. Real-world studies on fracture risk reduction are often limited by the use of indirect comparisons, short observational periods and missing information on bone mineral density.

Methods: This registry-based cohort study analysed anti-fracture effectiveness in a real-world population of patients from the osteoporosis register of the Swiss Society of Rheumatology who were treated with denosumab, bisphosphonates, or both sequentially. Fractures were analysed using event rates, rate ratios and hazard ratios (HR), including both denosumab and bisphosphonates as time-varying co-variates. Fracture risk hazards were adjusted (aHR) for baseline trabecular bone score (TBS) and T-scores at the lumbar spine, hip and 1/3 radius.

Results: A total of 3'068 patients (89% female, median age at treatment onset of 69 years [63 to 76]) received denosumab, bisphosphonates, or both sequentially. Thus, 11'078 subjects-years were assessed for bisphosphonates (41% alendronate, 36% ibandronate, 23% zoledronate) and 4'216 for denosumab. In addition, 48'375 subject-years were observed before treatment onset as well as 2'593 years of drug holidays. A total of 202 hip fractures (n = 67 under therapy), 1'482 vertebral fractures (n = 435 under therapy) and 2'262 major osteoporotic fractures (MOF; n = 692 under therapy) occurred after age 50. Crude HRs revealed no significant differences between denosumab and bisphosphonates in fracture risk reduction, but after adjusting for age, baseline T-scores and TBS, denosumab was associated with lower risk than bisphosphonates for vertebral fractures (aHR 0.63 (0.50 to 0.80), $p < 0.001$), MOF (aHR 0.74 (0.62 to 0.88), $p = 0.001$) and any fracture (aHR 0.76 (0.65 to 0.89), $p < 0.001$), but not for hip fractures (aHR 1.11 (0.68 to 1.84), $p = 0.67$).

Conclusions: When adjusting for disease severity, denosumab was associated with significant risk reduction compared to bisphosphonates for vertebral fractures and MOF, but not for hip fractures.

OP 3

Cell-free Mitochondrial DNA is a Reliable Biomarker in ANCA-Associated Vasculitides

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Background and aims: In anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV), ANCA recognize antimicrobial proteins and trigger neutrophil extracellular trap (NET) formation, which induce endothelial damage, vascular inflammation and necrosis (3). The aim of this study was to investigate the clinical utility of cell-free DNA quantification as a biomarker in AAV.

Methods: Total DNA was isolated from healthy controls (HC) and consecutive AAV plasma. Mitochondrial (mt) DNA and nuclear (n) DNA copy numbers were quantified by qPCR.

Results: Ninety-two HC (median age 51, 48% female) and 104 AAV patients (median age 64, 48% female, BVAS range: 0-40) were recruited. MtDNA plasma levels were significantly elevated in AAV ($8.7x10^7$ copies/ml), compared to HC ($6.7x10^6$copies/ml, $p < 0.0001$). nDNA levels did not differ. ROC analysis in patients with active AAV differentiated between AAV and HC with 96.1% sensitivity, 98.9% specificity and AUC of 0.99 at a $2.9x10^7$ copies/ml cut-off.

AAV patients with active disease (BVAS>0) had a mean of $2.0x10^8$ copies/ml of plasma mtDNA, significantly higher than HC ($p < 0.0001$) and patients in remission ($6.2x10^7$copies/ml, $p = 0.03$), whereas nDNA levels were similar.

A follow-up for 27 AAV patients showed that mtDNA level changes robustly correlated with changes in BVAS ($r = 0.56$, $p = 0.002$).

Conclusions: mtDNA, but not nDNA quantification allows a sensitive and specific distinction between HC and patients with AAV. mtDNA levels correlate cross-sectionally with disease activity in AAV patients. Plasma mtDNA quantification may therefore assist diagnosis and disease activity monitoring in AAV.

Declaration of conflict of interest: UW is coinventor of patents owned by Freiburg University; NV is coinventor of patents owned by Freiburg University

POSTERS

P 1

Comparison of drug retention of TNF inhibitors, other biologics and JAK inhibitors in patients with rheumatoid arthritis who discontinued JAK inhibitor therapy

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Objectives: JAK Inhibitors (JAKi) are recommended targeted synthetic (ts) disease modifying anti-rheumatic drugs (DMARDs) for patients with moderate-to severe rheumatoid arthritis (RA) who failed first-line therapy with methotrexate. Three different JAKis are currently licensed in Switzerland (Tofacitinib licensed in 2013, followed by Baricitinib 2017 and Upadacitinib 2020). There is a lack of data allowing an evidence-based choice of subsequent DMARD therapy for patients who had to discontinue JAKi treatment. We aimed to compare the effectiveness of TNF inhibitor (TNFi) therapy vs JAKi vs other mode of action (OMA) biologic DMARDs (bDMARDs) in RA patients who were previously treated with a JAKi.

Methods: RA Patients who discontinued JAKi treatment within the Swiss RA registry SCQM were included for this observational prospective cohort study. Primary outcome was drug retention for either TNFi, OMA bDMARD or JAKi, defined as the period between the treatment start and the stop date (date of last dose). The hazard ratio for treatment discontinuation was calculated adjusting for various potential confounders including ts/bDMARD history, previous type of ts/bDMARD and reason for discontinuation. A descriptive analysis of the reasons for discontinuation was performed.

Results: 400 treatment courses (TCs) of JAKi were included, with a subsequent switch to either JAKi, TNFi or OMA bDMARD. The crude overall drug retention was higher in patients switching to another JAKi (median retention time 918 days) as compared to TNFi (335 days) and OMA bDMARD (508 days). A significant difference of JAKi vs TNFi persisted after adjusting for potential confounders. The reason for discontinuation of the JAKi indicated by the treating rheumatologist was "not effective" in 57.2% (n = 229 TCs), "adverse events" in 27.8% (n = 111 TCs) and "other" in 15 %. The adverse events recorded in the database included 2 cases of pulmonary embolism, 2 cases of malignancy and one monoclonal gammopathy as events of special interest regarding JAKi treatment.

Conclusion: In a real-world population of RA patients who discontinued JAKi therapy, a switch to a second JAKi resulted in a higher drug retention as compared to switching to a TNFi. A switch to a second JAKi seems an effective therapeutic option and may be preferable over TNFi in patients who failed several bDMARD treatments.

P 2

BRD3 regulates the inflammatory and stress response in rheumatoid arthritis synovial fibroblasts

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Background: Small molecule inhibitors targeting members of the bromodomain and extra-terminal (BET) protein family (BRD2, BRD3, BRD4) have anti-inflammatory properties in rheumatoid arthritis (RA). BET proteins are readers of acetylated histone side chains and activators of transcription. BRD3 is an understudied member of BET proteins.

Objectives: To analyze the function of BRD3 in RA synovial fibroblasts (SF).

Methods: We cultured SF under hypoxic conditions (1% O2, 72h; n = 3) and mimicked oxidative stress with 4-hydroxynonenal (4-HNE; 5 µM, 48h; n = 4) and TNF (10 ng/ml, 48h). The expression of BRD3 was analyzed by Western blotting. We silenced the expression of BRD3 by lenti-viral transduction followed by TNF stimulation (10 ng/µl, 24h). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n = 3). Pathway enrichment analysis for KEGG and Reactome databases was conducted with significantly affected genes (± fold change >1.5, FDR <0.05). SF were treated with the bromodomain inhibitor I-BET (1 µM) and TNF (10 ng/µl, 24h). Autophagy was evaluated by Western blotting using the conversion of LC3B as a marker (n = 9).

Results: Hypoxia and oxidative stress suppressed the expression of BRD3 in presence of TNF. We detected 257 and 324 differentially expressed genes (DEG) that were affected by BRD3 silencing in unstimulated and TNF-stimulated SF, respectively. 105 DEG overlapped between the two groups. DEG were enriched in inflammatory pathways such as "TNF signaling pathway", "rheumatoid arthritis", "Toll-like receptor cascades", "MAPK signaling pathway", "IL-17 signaling pathway" and "signaling by interleukins". Furthermore, pathway enrichment analysis suggested a role for BRD3 in different stress-associated pathways, including "DNA repair", "chaperone mediated autophagy", "cellular responses to stress", and "autophagy". In line with the pathway enrichment analysis, I-BET induced levels of LC3B-II in unstimulated (4.3 fold, p = 0.07) and TNF-stimulated (2.9 fold, p = 0.07) SF, indicating a role of BET proteins in the regulation of autophagy.

Conclusion: BRD3 acts as an upstream regulatory factor that integrates the response to inflammatory stimuli and stress conditions in SF.

P 3

Effect of methotrexate and folic acid co-administration in arthritis

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Background: Methotrexate (MTX) is the first-line treatment for rheumatoid arthritis. Adjuvant-induced arthritis (AIA) rat is a robust model used to investigate arthritis. MTX reduces inflammation but is associated with adverse events. To reduce these side effects, folic acid (FA) is administrated at distance to MTX with no defined recommendation for its dosing (5-25mg/week) or time point of administration (1-3 days after MTX application). Whether the complicated therapeutic regimen with MTX once a week and FA at another time point affect compliance is an open question.

Objectives: The aim of this study was to assess the efficacy and tolerance of co-administration of MTX and FA compared to MTX with FA applied one day after MTX in the AIA.

Methods: Female Lewis rats received an injection of Mycobacterium butyricum defining day (D) 0 to induce arthritis. Treatment began on D9, one day before arthritis onset in this model. The first group of rats was treated with MTX only (n = 13), the second group received MTX and FA on the same day (n = 14), and the third group received FA one day after MTX administration (n = 14). MTX was administrated intraperitoneally at 1 mg/kg every 3 days and FA was delivered IP at 0.17 mg/kg. Arthritic index (AI) and ankle circumference (AC) were monitored. Micro-computed tomography of the ankle was performed to assess bone loss. Moreover, complete blood count, transaminases, and MTX-PG were assessed.

Results: Arthritis developed at D10 in all groups. AI and AC were similar in MTX groups at all time points. At D17, arthritis severity was lower in MTX groups (AI (mean and SD): 1.4 ± 1.6; AC: 35 ± 7 mm) compared to the control group (AI: 3.3 ± 0.6; AC: 42 ± 4 mm). Bone erosion and bone loss parameters were similar in all groups. Cortical porosity was around 0.40% ± 0.15 and bone volume/total volume was around 0.22% ± 0.13. MTX-PG1 was found at similar levels in MTX groups and correlated negatively with AI in MTX alone or MTX and FA at the same day groups ($p < 0.05$ and $p < 0.01$, respectively). Finally, white and red blood cells, platelets, hemoglobin, mean corpuscular volume, transaminases, and creatinine were found at a similar level in MTX groups.

Conclusions: Co-administration of MTX with FA on the same day is effective and well-tolerated compared to FA application one day after MTX. MTX metabolism was not affected. Thus, co-administration of MTX and FA seems to be possible and may be more convenient for the patients and improve compliance.

P 4

Early anti-S antibody levels predict anti-SARS-CoV-2 neutralizing activity over 24 weeks in RA patients after SARS-CoV-2 mRNA vaccination

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Objectives: Routine monitoring of vaccine-induced anti-S responses following mRNA based SARS-CoV-2 vaccination is not recommended routinely as uncertainties exist about the critical threshold of antibody levels that correlate to protection and the optimal timepoint for determination. In our study, anti-S antibody were analysed over 24 weeks following a standard two-dose regimen of mRNA based anti-SARS-CoV-2 vaccines and correlated to the development and persistence of neutralizing activity against SARS-CoV-2 in patients with rheumatoid arthritis (RA) on DMARD therapy compared to healthy controls (HC).

Methods: The RECOVER study was a prospective, controlled, monocentric study. Assessments were performed before vaccination, and at three, six, 12 and 24 weeks after the first vaccine dose.

Results: In RA patients, anti-S responses developed slower and resulted in lower peak titers compared to HC. A potent neutralizing activity (NT50) as assessed by a SARS-CoV-2 pseudoneutralization assay was observed in 60.3 % of all 73 RA patients and in all 21 HC after 12 weeks. A significant correlation between peak anti-S levels two weeks after the second vaccine dose and the development of a persistent neutralizing activity against SARS-CoV-2 was observed at week 12 and week 24. The analysis of IgG, IgA, and IgM isotype responses to RBD, S1, S2, and N proteins revealed a delayed IgG response, while IgA and IgM responses were maintained, suggesting a delayed isotype switch in RA patients.

Conclusions: Peak anti-S IgG levels two weeks after the second vaccine dose significantly predicted the development and persistence of a potent neutralizing activity against SARS-CoV-2 after 12 and 24 weeks. Our data suggest that the early determination of anti-S levels allows the timely identification of non- or poor-responding patients.

P 5

Effect of Zoledronate on Bone Mineral Density and Bone Turnover Markers after Long-term Denosumab Therapy: Observations in a Real-World Setting

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Background: The rebound effect after denosumab discontinuation is lessened with subsequent zoledronate therapy. However, it is unclear whether this mitigation is sufficient after long-term denosumab treatment.

Objective: This retrospective observational study analysed bone mineral density (BMD) and bone turnover marker (BTM) changes after denosumab therapy according to treatment duration and subsequent zoledronate regimen.

Methods: We measured the outcomes of 282 women with postmenopausal osteoporosis who discontinued denosumab and received zoledronate 6 months later.

In patients with longer denosumab therapy (≥5 years), BTMs were measured every 3 months and a second zoledronate infusion was administered if BTM levels increased by ≥2-fold. The BMD of all women was measured before denosumab therapy, at the last injection and 18-24 months later.

Results: Bone loss after switching from denosumab to zoledronate was higher in patients with a denosumab treatment duration of 4-6 years (n = 144) compared to 2-4 years (n = 84) (p <0.001 for lumbar spine and femoral neck), but there was no further increase with treatment durations of >7 years (n = 54) (p = 0.9 and p = 0.26, respectively). BTMs in patients with >5-year denosumab therapy were elevated 2-fold 6 months after the first zoledronate in some patients, but not all. Twenty-four women received a second zoledronate dose 6 months after the first one. BTMs in these patients were subsequently lower, but bone loss was comparable to patients with only one zoledronate dose.

Conclusions: Rebound-associated bone loss reached a plateau after denosumab treatment durations of 4-6 years, irrespective of the frequency of subsequent zoledronate therapy.

P 6

Risk of Osteonecrosis of the Jaw under Denosumab Compared to Bisphosphonates in Patients with Osteoporosis

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Background: Osteonecrosis of the jaw (ONJ) is a rare but serious adverse event associated with antiresorptive treatment. There is little evidence regarding the incidence of ONJ among patients with osteoporosis who are treated with denosumab versus bisphosphonates (BPs). The aim of this study was to determine the risk of ONJ in a real-world population.

Methods: Subjects who underwent at least one dual-energy X-ray absorptiometry (DXA) examination were included in the osteoporosis register of the Swiss Society of Rheumatology between January 1, 2015, and September 30, 2019. Statistical analyses included incidence rates, rate ratios and hazard ratios for ONJ, considering sequential therapies and drug holidays as time-varying covariates.

Results: Among 9'956 registered patients, 3'068 (89% female, median age 69 years [63 to 76]) were treated with BPs or denosumab for a cumulative duration of 11'101 and 4'236 patient-years, respectively. Seventeen cases of ONJ were identified; 12 in patients receiving denosumab at the time of ONJ diagnosis and five in patients receiving oral or intravenous BP therapy. The diagnosis of ONJ was confirmed by independent and blinded maxillofacial surgeons, using the American Association of Oral and Maxillofacial Surgeons case definition of ONJ. The incidence of ONJ per 10'000 observed patient-years was 28.3 in patients receiving denosumab and 4.5 in patients with BP-associated ONJ, yielding a rate ratio of 6.3 (95% CI: 2.1 to 22.8), p <0.001. Nine of 12 patients who developed ONJ during denosumab treatment had been pretreated with BPs, but none of the five patients with BP-related ONJ had previously received denosumab. The risk of ONJ was higher in patients receiving denosumab therapy compared to BPs (hazard ratio 3.49, 95% CI: 1.16 to 10.47, p = 0.026). Previous BP therapy before switching to denosumab may be an additional risk factor for ONJ development.

Conclusion: The risk of ONJ was higher in patients receiving denosumab therapy compared to BPs. Previous BP therapy before switching to denosumab may be an additional risk factor for ONJ development.

P 7

Developing a Screening Tool for the Detection of Interstitial Lung Disease in Systemic Sclerosis: the ILD-RISC Score

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Background: Some physicians do not regularly screen for systemic sclerosis associated interstitial lung disease (SSc-ILD) with computed tomography (CT) at SSc diagnosis. In addition, it is unclear according to which criteria HRCTs should be repeated in the follow-up of baseline ILD negative cases. We aimed to develop a risk score for the presence of SSc-ILD (the ILD-RISC score), to guide physicians in ordering both baseline and follow-up CTs.

Methods: The steering board (six experts, two fellows and a patient research partner) used the nominal group technique to select items for regression analysis according to face validity, feasibility, scientific background and personal experience. The prediction model for the presence of ILD was developed from baseline visits using multivariable logistic regression with backward selection. Patients were randomly divided into 66% derivation and 34% validation cohorts. Missing data in the selected covariates or in the ILD status determined exclusion. After identifying a cut-off favoring sensitivity >85% from the ROC curve analysis, the ILD-RISC score was applied in the validation cohort and then longitudinally in a cohort of SSc patients with negative baseline HRCT.

Results: The steering board selected 13 variables: sex, age, disease duration, skin subset, esophageal symptoms, digital ulcers (DU) ever, arthritis ever, smoking ever, increased ESR/CRP, NYHA class, SSc autoantibody (SSc_Atb), FVC% and DLCO%. In the derivation cohort (533 patient, 43% ILD), the ILD-RISC model including FVC%, DLCO%, DU ever, age and SSc_Atb showed an AUC of 79.1% (75.3-83.0%) for the presence of ILD on HRCT. An ILD-RISC score≥0.3 showed sensitivity 85.6% and specificity 53.6%, which were replicated in the validation cohort (247 patients, 48% ILD, AUC 76.4%, sens. 85.7%, spec. 49.2%). Among 819 patients with negative baseline CT, 170 developed ILD during a 3.8?3.0 years follow up. Longitudinally, the ILD-RISC score showed comparable performance (AUC 72.6%, sens. 80.4%, spec. 50.5%): in almost 50% of visits (n = 914/1809) the CT could be correctly skipped following an ILD-RISC score <0.3.

Conclusion: We developed and validated the ILD-RISC score to predict the presence of ILD at time of the visit. The ILD-RISC may be useful in routine practice when resources for CTs might be limited. Most importantly, it may also help to decide when to order CTs at follow up, thus limiting unnecessary CTs and reducing the burden for patients and institutions.

P 8

Long-term effect of tocilizumab monotherapy after ultra-short glucocorticoid administration to treat giant cell arteritis – one year-follow up of the GUSTO Trial

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Background: Two randomised controlled trials (RCT) [1, 2] demonstrated a glucocorticoid (GC)-sparing effect of tocilizumab (TCZ) of at least 50%. The GUSTO (giant cell arteritis (GCA) treatment with ultra-short GC and TCZ) trial was set up to evaluate the efficacy and safety of TCZ-monotherapy after ultra-short GC treatment in new-onset GCA. Data up to week 104 is presented.

Objectives: To explore the maintenance of efficacy 1 year after discontinuation of TCZ treatment and the effectiveness of retreatment with TCZ after relapse.

Methods: Eighteen patients with newly diagnosed GCA were enrolled in this investigator-initiated, single-arm, single-center, open-label clinical trial [3]. Patients received 500 mg methylprednisolone intravenously for 3 consecutive days. Thereafter, GC treatment was discontinued and TCZ was administered intravenously, followed by weekly subcutaneous TCZ injections from day 10 until week 52. Patients in clinical remission stopped TCZ at week 52 and entered follow-up. Maintenance of efficacy at week 104 included the proportion of patients with complete relapse-free remission of disease at week 104, and time to first relapse after week 52.

Results: At baseline there were 12/18 female patients, and the median age was 72 (range 67-75) years. Overall, 15/18 had cranial symptoms (10/18 had jaw claudication, 6/18 had visual symptoms), 10/18 suffered from polymyalgia rheumatica-symptoms, 16/18 had positive cranial ultrasound, and 13/18 had positive histopathology at any time before study inclusion. At week 52, 13/18 patients were in relapse-free remission and entered follow-up. 1/13 patients presented with a minor relapse (at week 72). Remission was achieved in this patient after restart of TCZ-monotherapy. At week 104, 12/18 patients were in relapse-free remission.

Conclusion: After a 3-days pulse of methylprednisolone followed by 52 weeks of TCZ monotherapy, drug-free remission was maintained until week 104 in all but one patient entering long-term extension (12/13, 92%). The relapse rate after treatment discontinuation was substantially lower than reported in the RCTs [1,2]. This high drug-free remission rate may – at least in part – be explained by the patient characteristics (exclusively new diagnoses), and the 3-day GC pulse. Based on the study design, the treatment procedure should not be used in everyday clinical practice.

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P 9

Persistent inflammation in systemic sclerosis is strongly associated with severe disease and mortality: an analysis from the EUSTAR database

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Background: A subset of patients with systemic sclerosis (Ssc) show elevated CRP levels (20-35%), which has been reported as inflammatory SSc. Preliminary data suggest that this subset is characterized by a severe phenotype.

Objectives: To analyse the phenotype and the survival of inflammatory compared with non-inflammatory SSc patient subsets.

Methods: Data from 8571 SSc patients with available CRP measurement from the EUSTAR cohort were analysed. Exclusion criteria included acute infection, missing follow-up and tocilizumab treatment. Patients with a CRP ≥5mg/l at ≥80% of visits were stratified as persistent inflammatory and as non-inflammatory if CRP was ≥5 mg/l at <20% of visits (1). As a sensitivity analysis, patients were defined as inflammatory and non-inflammatory based on a single CRP measurement at baseline only (CRP ≥5 or <5mg/l). Kaplan Meier curves with log-rank tests were used to estimate time from baseline to death and Cox regression to compare mortality risks adjusted for time from diagnosis to baseline.

Results: Out of 2883 patients with more than two visits, 404 (14%) showed persistent inflammation and 1032 (36%) a non-inflammatory phenotype. Out of 5619 patients with more than one visit, 1830 (33%) were stratified as inflammatory as defined by as single CRP measurement at baseline, 3789 (67%) as non-inflammatory. With both definitions, the inflammatory subset revealed a more severe phenotype than non-inflammatory patients, including more frequent diffuse-cutaneous disease, anti-Scl-70 autoantibodies, pulmonary fibrosis, pulmonary hypertension, higher modified Rodnan skin score, and lower forced vital capacity and diffusing capacity for carbon monoxide. Patients with persistent inflammation had a strongly increased risk of all-cause mortality (HR 7.1 [95%CI 3.7 to 13.5], p <0.001) compared to non-inflammatory patients, whereas this association was weaker when based on a single CRP measurement (HR 2.6 [95%CI 2.1 to 3.2], p <0.001).

Conclusion: The severe phenotype and decreased survival of the inflammatory SSc subset, which was most prominent in patients with persistently elevated CRP levels, suggest a distinct disease subset. Therefore both, the need for more regular monitoring of inflammatory parameters and implications for immune-modulating treatment, needs to be carefully analysed.

Reference

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P 10

Radiomic signatures reflect treatment response to nintedanib in a preclinical lung fibrosis model

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Evaluation of anti-fibrotic drugs in preclinical models of lung fibrosis by histological analysis is often error-prone due to spatial disease heterogeneity. Quantitative analysis of biomedical imaging features, called "radiomics", may represent a more accurate measure because it can capture whole organ pathology on both spatial and temporal level. We studied the potential of µCT-derived radiomic features to reflect response to nintedanib in the bleomycin (BLM)-induced murine lung fibrosis model. Lung fibrosis was induced in C57BL/6J mice by intratracheal instillation of 2 U/kg BLM. Treatment with 60 mg/kg nintedanib (n = 10) or vehicle (n = 14) was provided daily by gavage from day 7 to 21. Whole-lung µCT scans at 35 µm resolution of each mouse were acquired at baseline (day 0), pre- (day 7), and post-treatment (day 21). Mice were sacrificed on day 21 for collection of lung tissue. Treatment effects were assessed by Ashcroft score on lung tissue sections. Radiomic features, describing histogram, texture, and wavelet characteristics, were extracted from 3D lung volumes resized to 0.15 mm isotropic voxels using our in-house software Z-Rad. Following data pre-processing, agglomerative clustering of temporal feature trajectories was done on nintedanib-treated samples to identify distinct clusters. Cluster behavior was then compared between study groups. Ashcroft scoring did not reveal a significant difference between nintedanib (3.1 ± 1.1 s.d.) and vehicle-treated (3.5 ± 1.0 s.d.) mice. Agglomerative clustering of radiomic features revealed two distinct clusters composed of 50 (cluster 1) and 68 (cluster 2) features. Comparison of mean feature value trajectories revealed a significant decrease upon treatment in cluster 1 only for nintedanib samples ($p < 0.01$), which were additionally separated from vehicle samples at post-treatment conditions ($p < 0.05$). In contrast, mean feature values in cluster 2 remained flat for both groups upon treatment ($p > 0.05$). Interestingly, we found similar behavior for a cohort of nintedanib (n = 5) and vehicle-treated (n = 5) samples from an independent experiment with analogous study setup. The results suggest that radiomic features identified differences on imaging level following nintedanib treatment, which we could not reliably detect on tissue level using Ashcroft scoring. These findings hold potential for the development of novel image-based readouts for improved stratification of anti-fibrotic treatment effects in lung fibrosis models.

P 11

Understanding the flexion-relaxation phenomenon in patients with chronic nonspecific

low back pain through virtual real

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The flexion-relaxation phenomenon (FRP), a myoelectric silence occurring when the trunk is fully flexed, is frequently absent in patients with non-specific chronic low back pain (LBP). However, it is unknown whether the absence of FRP in patients with LBP is intrinsic to the pathology or merely a consequence of reduced trunk flexion. Immersive virtual reality (IVR) can create an avatar whose range of motion can be modulated to differ from the real movement. This study aimed to use IVR to modulate trunk range of motion (ROM) in participants unaware of the modulation and observed the effect on the FRP. Fifteen patients with LBP and fifteen asymptomatic participants (AP) matched in age were enrolled and equipped with 34 reflective markers. Trunk kinematics were assessed with an optoelectronic system. FRP was assessed with active surface electromyography electrodes positioned bilaterally lumbar erector spinae longissimus. In VR conditions, participants wore a head-mounted display with which they embodied an avatar existing in a virtual environment. The motion capture created an avatar streamed in real-time to the 3D IVR software and displayed through the head-mounted display. The virtual environment was composed of only a closed room, a mirror, and within the mirror, a target line to be reached by trunk flexion. The avatar trunk movements were modulated from reality into five IVR conditions by applying scaling factors ranging from 0.667 to 1.19 (<1 = increased ROM; >1 = decreased ROM). Participants were unaware of these modulations. First, participants performed three maximal trunk flexions without IVR setting to establish a control condition for defining maximal trunk range of motion (ROM). Then, they were equipped with the IVR setting and were asked to flex their trunk until reaching the target line. Two trials per condition were required and the order of the 5 IVR conditions was randomly selected. First of all, none of the participants of both groups perceived the modulation. Then, Modulated IVR condition successfully allowed both groups AP and LBP to significantly increase their flexion angle. In LBP patients, the increase in flexion angle significantly influenced the ratio of FRP. The absence of FRP in the LBP population appears to be primarily related to the reduced range of motion. Successful modulation of ROM makes IVR a promising tool to better understand neuromuscular modifications recorded in LBP patients and could be used for rehabilitation.

P 12

Rhematoid arthritis and sarcopenia – a prospective single center cohort study in postmenopausal women

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Background: Rheumatoid arthritis (RA) can cause significant impairment of soft tissues but longitudinal cohort data on the risk of sarcopenia are scarce.

Methods: We measured changes in appendicular lean mass index (ALMI, Kg/m2) by dual-energy x-ray absorptiometry (DEXA) and handgrip strength by dynamometer (mmHg) in postmenopausal women, 71 RA patients and 84 healthy controls (HC), over a median follow-up of 2.2 years (IQR 2.0 - 7.3). We defined low muscle mass as ALMI ≤ 5.5 Kg/m2 and sarcopenia as ALMI ≤ 5.5 Kg/m2 plus handgrip strength <174 mmHg. We calculated linear regression models including demographic and anthropometric data, comorbidities, and co-medication as confounders.

Results: Median age was 61 (IQR 55 - 69), median RA disease duration 13 (IQR 6 - 25) years. Median ALMI at baseline was 6.3 (IQR 5.9 - 6.6) Kg/m2 in RA patients and 6.3 (IQR 5.7 - 6.8) Kg/m2 in HC ($p = 0.89$). Prevalence of low muscle mass was 15.8 % in RA patients and 16.7 % in HC. Prevalence of sarcopenia was 14.3 % in RA patients and 0 % in HC. In the fully adjusted model (n = 132), median change in ALMI per year was -0.04 (95%CI -0.08 to -0.0) Kg/m2 in RA patients versus 0.02 (95%CI -0.01 to 0.04) Kg/m2 in HC resulting in a differential loss of muscle mass in RA patients of -0.06 (95%CI -0.11 to -0.1) Kg/m2 per year ($p = 0.013$).

RA patients had an OR of 1.36 (95%CI 1.12 - 1.67) for experiencing any loss of muscle mass during the study period compared to HC (p = 0.002). Loss of muscle mass in RA patients was driven by those with normal muscle mass at baseline. RA patients with low muscle mass at baseline did not experience a decline in muscle mass.

Except for the use of TNFα inhibitors (ALMI difference -0.08 [95%CI -0.01 to -0.16] Kg/m2, p = 0.021), neither drug therapy nor disease duration were independently associated with loss of muscle mass in RA patients.

Conclusion: We found an increased risk for declining muscle mass in postmenopausal women with long-lasting RA compared to HC. However, our results suggest that magnitude of muscle loss is very small and clinical significance highly questionable. In addition, our results suggest, that low muscle mass is not a given predictor for accelerated future decline in postmenopausal women with RA.

P 13

Effectiveness of a one-week inpatient multimodal pain treatment program for patients with rheumatologic diseases and musculoskeletal pain – a single center observational study

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Background: Multimodal rheumatologic complex treatment (MRCT) is a treatment concept for patients with rheumatologic diseases requiring acute inpatient care suffering from exacerbated pain and/or functional impairment. A rheumatologist directs the treatment program including multimodal assessments and treatment from three of the following: ergotherapy, physiotherapy, pain medicine and cognitive behavioural treatment.

Objective: To evaluate the effectiveness of a one-week inpatient MRCT on musculoskeletal pain and function of patients with rheumatologic disorders.

Methods: 59 consecutive patients were entered into a program of multimodal treatment courses from January 2021 until December 2021. Two patients were excluded for evaluation (one patient acquired COVID-19 during hospitalization and one patient was excluded due to missing data). Pain was assessed via visual analogue scale (VAS) and functional impairment via the "Funktionsfragebogen Hanover (FFbH)" and the "Health Assessment Questionnaire (HAQ)" at admission, at discharge and at 12 weeks of follow up. Paired t-test analyses for all treatment episodes were performed.

Results: The mean treatment duration (days, ±SD) was 8.1 ± 0.8. Mean age (years, ±SD) of the 57 patients treated in the MRCT program was 57.2 ± 12.5, with 72% female and 28% male patients. Of all patients, 40% had an underlying inflammatory disorder, 60% a non - inflammatory rheumatic disease. 23% of all patients had "back pain", 14% "spondyloarthritis" and 11% "rheumatoid arthritis". VAS (pain) mean at admission was 6.9 ± 1.0 (SD), HAQ mean 0.57 ± 0.23 (SD) and FFbH mean 81.44 ± 7.95 (SD), respectively. Significant improvements in VAS, HAQ and FFbH were demonstrated at discharge, with a mean improvement of VAS of -2.86 (95% CI: -3.07 to -2.64, P value: <0.0001), a mean improvement of HAQ of -0.24 (95% CI: -0.28 to -0.20, P value: <0.0001) and a mean improvement of FFbH of 5.38 (95% CI: 3.78 to 6.98, P value: <0.0001). Follow up assessment at week 12 was recorded in 22 patients (39%) with a significant mean improvement in VAS of -2.23 (95% CI: -2.98 to -1.48), P value <0.0001).

Conclusion: Significant improvement of pain and function was demonstrated at discharge and at week 12 in patients with rheumatologic diseases and musculoskeletal pain completing a one-week inpatient multimodal interprofessional treatment program. A multimodal therapeutic approach may provide an effective treatment strategy superior to unimodal standard management.

P 14

Evidence based clinical practice guideline for follow-up care after spinal cord injury

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Background: Prevalence of secondary health conditions (SHC) in persons with spinal cord injury (SCI) is high and life expectancy of persons with SCI is still lower compared to able-bodied persons. Although it is established that follow-up care programs across the life span prevent health problems, current follow-up care programs are mostly expert opinion based and vary widely regarding content, frequency and setting. In order to provide patients with SCI up-to-date and best possible medical and rehabilitative care, an evidence based clinical practice guideline (CPG) for follow-up care is needed.

Method: By establishing a guideline conform to the guidance of AWMF (Association of the Scientific Medical Societies in Germany) a systematic review was performed to:

1. Search for existing guidelines and literature for follow-up care programs and a methodological appraisal. All guidelines were evaluated according to the DELBI (German Guideline rating system) and literature according to the Scottish Intercollegiate Guideline Network (SIGN)

2. Define secondary health problems based on existing literature and expert opinion to be included in the CPG (prevalence, severity, modifiability)

3. Define population and sub-populations, frequency and setting of follow-up care and suggested outcome measures based on current evidence

After a structured consensus process with SCI specialists and country representatives of patient associations, level of evidence and grading of recommendation were defined.

Results: The systematic review found 62 guidelines, 48 Cochrane reviews and 2963 publications. After title and abstract screening, 79 publications were full text read by two independent reviewers. All guidelines and publications were checked for their suitability and, if included, rated according to the AWMF guidance. None of the guidelines or papers described an evidence based CPG for follow-up care. A second review of existing guidelines and literature was performed resulting in the definition of the following health problems that need to be included in the CPG: 1. Nervous System 2. Pain 3. Cardiovascular system 4. Respiratory System 5. Immune system 6. Digestive tract 7. Endocrine system and Nutrition 8. Urogenital system 9. Pregnancy and Birth 10. Musculoskeletal System 11. Skin 12. Psychological Problems 13. Medication and Polypharmacie

Discussion: Based on this, a CPG for follow-up care across the lifespan including content, frequency and setting of follow-up care was defined.

P 15

Retrospective study of the clinical characteristics of symptomatic COVID-19 infections of individuals with paraplegia

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Introduction: Since the beginning of 2020, the treatment of Covid-19 patients has been a major challenge in medical everyday life. It is unclear whether the clinical course is more severe in individuals with spinal cord injury (SCI) compared to the general population. While certain studies indicate that individuals with SCI have a higher mortality rate and a higher level of infection with COVID-19 than the general population [1], other studies make it clear that the disease courses are by no means more severe [2].

The aim of this study is to describe the clinical course and length of stay of individuals with SCI and symptomatic Covid-19 infection who required hospital admission to the Swiss Paraplegic Center (SPC).

Methods: Retrospective data analysis of clinical data of individuals with SCI who were hospitalized with Covid-19 at the SPC from March 01, 2020 to December 31, 2021.

Results: During the mentioned period, 13 individuals with symptomatic Covid-19 infection were hospitalized at the SPC. Of these, 61% were male (n = 8), and the mean age was 59 years (SD 15 years). 60% had a tetraplegia (46% incomplete) and 40% had a paraplegia (54% incomplete). The mean length of stay was 19 days (SD 9.03). Six individuals were treated in the intensive care unit, all of whom were persons with paraplegia.

Persons with paraplegia tended to have a longer length of stay (26 SD 5.8) than persons with tetraplegia (13.75 SD 7.6). Two persons (both with a tetraplegia) died during the hospital stay (15%).

Conclusion: These data provide initial insight into the course of symptomatic Covid-19 infection in individuals with SCI and provide a basis for further research projects.

Literature

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P 16

Impact of Serologic Status on Clinical Responses to Upadacitinib or Abatacept in Patients with Rheumatoid Arthritis and Prior Inadequate Response to Biologic DMARDs: Sub-Group Analysis from the Phase 3 SELECT-CHOICE Study

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Background: In pts with RA who had a prior inadequate response or intolerance to bDMARDs, the oral JAKi upadacitinib (UPA) demonstrated superiority in change from baseline in DAS28(CRP) and DAS28(CRP)<2.6 at week 12 and improved responses across additional endpoints compared to abatacept (ABA) in the phase 3 SELECT-CHOICE study. Seropositive pts have been reported to respond better to treatment than seronegative pts. The objective of this sub-group analysis was to evaluate clinical responses with UPA versus ABA among RA pts based on serologic status.

Methods: In SELECT-CHOICE, RA pts were randomized to oral UPA or intravenous (IV) ABA. For this sub-group analysis, pts were categorized as follows: RF+ and ACPA+, RF+ and/or ACPA+, and RF- and ACPA-. Mean change from baseline in DAS28(CRP), Clinical Disease Activity Index (CDAI), ACR responses, HAQ-DI, patient's assessment of pain, and Functional Assessment of Chronic Illness Therapy - Fatigue scale (FACIT-F) were evaluated at weeks 12 and 24. Statistical inference was conducted using Chi-square tests or analysis of covariance (ANCOVA) with non-responder imputation or multiple imputation used for missing data and nominal P-values shown.

Results: Of the total population (N = 612), the majority of pts were seropositive for RF and/or ACPA at baseline (80.4%). Most pts were female (~80%), ~55 years old, and one-third had previously experienced ≥2 bDMARDs. Mean change from baseline in DAS28(CRP) and CDAI were numerically higher with UPA vs ABA at weeks 12 and 24 across all sub-groups. Regardless of serologic status, UPA demonstrated numerically higher responses vs ABA for ACR 20/50/70 and proportions of patients in low disease activity and remission at both timepoints. Mean change from baseline in the HAQ-DI and the patient's assessment of pain was numerically higher with UPA compared to ABA across all sub-groups and timepoints. Clinical responses were generally numerically higher at week 24 compared to week 12, and for the seropositive groups compared to the seronegative group, with both UPA and ABA.

Conclusions: Across serologic statuses, clinical responses with UPA 15 mg vs ABA were numerically higher at weeks 12 and 24 among RA pts with prior inadequate response or intolerance to bDMARDs. In addition, clinical responses were numerically higher for seropositive pts compared to seronegative pts across all endpoints assessed, although the seronegative group had a smaller sample size in this post-hoc analysis.

P 17

Consistency in Time to Response with Upadacitinib as Monotherapy or Combination Therapy and across Patient Populations with Rheumatoid Arthritis

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Background: Upadacitinib (UPA) has demonstrated efficacy in pts with moderate-to-severe RA across various populations. This post hoc analysis aimed to evaluate the consistency in time to achieving meaningful clinical response with UPA 15 mg + csDMARDs in bDMARD-inadequate responder (IR) versus csDMARD-IR pts with RA as well as with UPA 15 mg mono versus UPA 15 mg + csDMARDs in csDMARD-IR pts.

Methods: Pts originally randomized to UPA 15 mg once daily from 4 Phase 3 trials were included in this analysis: SELECT-BEYOND and SELECT-CHOICE (UPA 15 mg + csDMARDs in bDMARD-IR pts), SELECT-NEXT (UPA 15 mg + csDMARDs in csDMARD-IR pts), and SELECT-MONO (UPA 15 mg mono in MTX-IR pts). Time to response was estimated using the Kaplan–Meier method for clinical outcomes over 24 weeks (26 weeks in SELECT-MONO). Clinical

outcomes included achievement of DAS28[CRP] ≤3.2; low disease activity (LDA) defined as CDAI ≤10 and SDAI ≤11; and 50% improvement in ACR core components and morning stiffness (MS) duration/severity. Data presented were as observed.

Results: Overall, 905 pts were included (SELECT-BEYOND: n = 164; SELECT-CHOICE: n = 303; SELECT-NEXT: n = 221; SELECT-MONO: n = 217). csDMARD-IR pts had a mean disease duration of 7.3 (SELECT-NEXT) or 7.5 years (SELECT-MONO); bDMARD-IR patients had a mean disease duration of 12.4 years, with a more refractory population (≥3 prior bDMARDs) in SELECT-BEYOND (23%) than SELECT-CHOICE (10%). In general, the median time to DAS28(CRP) ≤3.2, CDAI LDA, 50% improvement in ACR core components, and 50% improvement in MS duration/severity were consistent across the studies in bDMARD-IR and csDMARD-IR pts. For SELECT-BEYOND, SELECT-CHOICE, SELECT-NEXT, and SELECT-MONO, the median (95% CI) time to achieve DAS28(CRP) ≤3.2 was 12 (12, 16), 12 (8, 12), 12 (8, 12), and 14 (8, 14) weeks, respectively, and the median time to achieve CDAI LDA was 20 (12, 24), 16 (12, 16), 16 (12, 16), and 20 (14, 20) weeks, respectively. A longer median (95% CI) time to achieve SDAI LDA was observed with UPA mono (20 [14, 20] weeks) versus UPA + csDMARDs (12 [12, 16] weeks) in csDMARD-IR pts. Among bDMARD-IR pts, the median (95% CI) time to 50% improvement in pain was longer in SELECT-BEYOND versus SELECT-CHOICE (16 [12, 20] versus 8 [8, 12] weeks).

Conclusion: In diverse populations with RA, pts treated with UPA 15 mg, as mono or with csDMARDs, generally demonstrated consistent time to achieving DAS28(CRP) ≤3.2, CDAI LDA, and 50% improvement in clinical outcomes.

P 18

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

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Background: The SELECT-CHOICE trial of pts with RA and prior inadequate response (IR) to bDMARDs demonstrated superiority of the JAKi 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.

Objective: To evaluate the impact of UPA vs ABA on individual components of composite measures of disease activity in SELECT-CHOICE.

Methods: In SELECT-CHOICE, a double-blind phase 3 trial, bDMARD-IR patients were randomly assigned to UPA 15 mg once daily or ABA. 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 (the lowest of percent change in TJC, percent change in SJC, or median of the other 5 ACR components) were determined using the Kolmogorov-Smirnov test and are reported as observed. For all other variables, non-responder imputation 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 in SELECT-CHOICE (UPA 15 mg, n = 303; ABA, n = 309). 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 patients receiving UPA and ABA achieved ≥50% improvements in all but the hsCRP component. Overall, 15% and 26% of patients 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 patients on UPA vs 2% and 10% of patients on ABA. 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 patients, 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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Efficacy and safety of upadacitinib in TNFi-IR patients with rheumatoid arthritis from three Phase 3 clinical trials

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Background: For pts with RA who are refractory to bDMARDs, such as TNFis, optimal disease control is less likely to be achieved with subsequent therapy. In line with recommendations from EULAR and ACR, switching to a treatment with a different mechanism of action is appropriate for these pts.

Objectives: To describe the efficacy and safety of upadacitinib (UPA) 15 mg once daily in pts with RA and an inadequate response or intolerance to TNFis (TNFi-IR).

Methods: A post hoc subgroup analysis was conducted in TNFi-IR pts who were treated with UPA 15 mg once daily in 3 Phase 3 clinical trials: SELECT-BEYOND, -CHOICE, and -COMPARE. For COMPARE, only patients treated with adalimumab and switched to UPA as rescue therapy were included. ≥20/50/70% improvement in ACR criteria, DAS28-CRP, CDAI, and SDAI as well as change from baseline in HAQ-DI and other patient-reported outcomes (PROs) were reported through 24 weeks. Non-responder imputation was used for all missing categorical outcomes; as observed (COMPARE) or multiple imputation (CHOICE, BEYOND) were used for missing continuous outcomes. Pooled safety results were presented as exposure-adjusted event rates (EAERs) with a cut-off of June 30, 2021.

Results: 568 TNFi-IR pts were included: 146 from BEYOND, 263 from CHOICE, and 159 from COMPARE. Mean duration since RA diagnosis was longer for BEYOND and CHOICE versus COMPARE; CV risk factors were common among this refractory population. ACR20/50/70 and disease activity outcomes observed in the TNFi-IR population were generally consistent with the overall BEYOND and CHOICE bDMARD-IR populations, and consistent across the 3 studies in the TNFi-IR subgroups. Improvements in PROs including HAQ-DI, fatigue, pain, and morning stiffness over 24 weeks were observed (data not shown).

Pooled safety results reporting 1574.8 PY of exposure in the TNFi-IR subgroup showed similar results to the overall BEYOND and CHOICE bDMARD-IR study populations, with EAERs of 3.1 events/100 PY for herpes zoster and 0.8 events/100 PY for adjudicated major adverse CV events and venous thromboembolism, and malignancy excluding non-melanoma skin cancer. The EAER of any AE leading to death was 1.4 events/100 PY.

Conclusions: In this post hoc subgroup analysis, TNFi-IR pts treated with UPA 15 mg achieved clinically meaningful efficacy responses over 24 weeks, with safety consistent with the overall bDMARD-IR population in the Phase 3 program.

P 20

Long-Term Safety Profile of Upadacitinib in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis

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Background: The efficacy and safety of the oral JAKi upadacitinib (UPA) has been evaluated for several rheumatic diseases. The objective of this analysis is to describe the long-term safety profile of UPA across RA, PsA, and AS from the SELECT clinical program.

Methods: Safety data (cut-off: 30 June 2020) from the UPA SELECT clinical program were compiled for RA (6 trials), PsA (2 trials), and AS (1 trial) for this analysis. Treatment-emergent adverse events (TEAEs; onset on or after first dose and ≤30 days after last dose for UPA and methotrexate [MTX] or ≤70 days for adalimumab [ADA]) were summarized for RA (pooled UPA 15 mg once daily [QD], ADA 40 mg every other week [EOW], and MTX), PsA (pooled UPA 15 mg QD and ADA 40 mg EOW), and AS (UPA 15 mg QD). TEAEs are reported as exposure-adjusted adverse event rates (EAERs; events/100 patient-years [E/100 PY]).

Results: In total, 4298 patients (RA, N = 3209; PsA, N = 907; AS, N = 182) received ≥1 dose of UPA 15 mg, totaling 8562 PY of exposure, with the majority of exposure from RA studies. AEs leading to discontinuation were generally similar across all treatment groups (UPA, ADA, and MTX) and patient populations (RA, PsA, and AS). Rates of serious infection and opportunistic infection were generally similar across all treatment groups within each population and across RA, PsA, and AS. No serious infections were reported in patients with AS. Herpes zoster and increased CPK were reported more often with UPA compared to ADA or MTX, with UPA showing similar rates of herpes zoster across RA, PsA, and AS. Malignancies excluding NMSC were reported at similar rates across all treatment groups and populations. NMSC was not common, with numerically higher rates observed with UPA versus MTX and/or ADA in RA and PsA. Similar rates of adjudicated MACE and adjudicated VTE were observed across all treatment groups, with no events reported in patients with AS. Rates of death reported in these clinical studies were not higher than expected in the general populations. As anticipated for the patient populations, the most common cause of death observed was cardiovascular in nature.

Conclusions: With the exception of herpes zoster, EAERs were generally similar across UPA, ADA, and MTX in RA, as well as UPA and ADA in PsA. No new safety risks were identified with long-term treatment in RA, PsA, or AS. UPA 15 mg demonstrated a consistent safety profile across RA, PsA, and AS populations in the SELECT clinical program.

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Clinical Outcomes Associated with Glucocorticoid Discontinuation Among Patients With Rheumatoid Arthritis Receiving Upadacitinib or Adalimumab

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Background: Pts with RA are often administered glucocorticoids (GCs) as bridging therapy when initiating or adjusting DMARDs. Due to their systemic effects, short-term use of GCs at the lowest possible dose is recommended with rapid tapering.

Objectives: We describe GC discontinuation patterns and the associated clinical outcomes in pts with RA receiving upadacitinib (UPA) or adalimumab (ADA).

Methods: SELECT-COMPARE is a randomized phase 3 trial of UPA vs placebo and ADA with a 48-week (wk) double-blind treatment period and a 10-year long-term extension in pts with RA receiving concomitant methotrexate (MTX) who had an inadequate response to MTX.Background GCs (≤10 mg/day prednisone or equivalent) were permitted and could be tapered or discontinued starting at wk 26 per physician discretion. This post hoc analysis included pts who received ≥1 dose of UPA 15 mg once daily or ADA 40 mg every other wk while on concomitant GCs at baseline. The proportion of pts with disease worsening (CDAI >2 and DAS28-CRP >0.6) following GC discontinuation through follow-up is described. Maintenance of clinical response, including remission and low disease activity based on CDAI ≤2.8 and ≤10, respectively, as well as DAS28-CRP <2.6 and ≤3.2, were assessed among pts who discontinued GCs. Adverse events (AEs) were assessed before and after GC discontinuation through follow-up.

Results: Of 1,629 pts randomized, 978 (60%) used GCs at baseline; 128 (13%) discontinued use at/after wk 26 (UPA, n = 97; ADA, n = 31). Median follow-up time after GC discontinuation was 60 wks for UPA and 84 wks for ADA. At the time of GC discontinuation, a numerically higher proportion of pts treated with UPA vs ADA were in disease control (CDAI ≤2.8: 55% vs 32%; CDAI ≤10: 85% vs 68%; DAS28-CRP <2.6: 71% vs 48%; DAS28-CRP ≤3.2: 87% vs 62%). Few pts receiving UPA experienced disease worsening following GC discontinuation (1% CDAI increase >2; 7% DAS28-CRP increase >0.6) and none on ADA. At 6 months follow-up after GC discontinuation, most pts treated with UPA and ADA maintained CDAI ≤2.8 (74% vs 88%) and ≤10 (92% vs 95%) and DAS28-CRP <2.6 (89% vs 85%) and ≤3.2 (91% vs 94%), respectively. GCs were reintroduced (albeit usually temporarily) in 14% of pts on UPA and 19% on ADA. AEs were generally similar across treatment groups.

Conclusion: In pts who achieved disease control and discontinued GCs, disease control was maintained in almost all without worsening disease activity over time.

CASES

Case 1

Tuberculous arthritis unveiled by somatostatin analogue radioligand therapy

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A 72-year-old woman with a 3-year history of metastatic pancreatic Neuro-Endocrine Tumour (NET) was hospitalised for chronic right ankle monoarthritis. Eight months before admission, she was started on [Lutetium-177-DOTA0,Tyr3]octreotate (^{177}Lu-Dotatate), a radiolabeled somatostatin analogue, administered intravenously every 8 weeks for a total of 4 doses. One month after the first infusion, she reported pain and swelling of her right ankle followed by spontaneous resolution. Her ankle symptoms relapsed after each of the three consecutive ^{177}Lu-Dotatate infusions. Two synovial fluid analyses revealed low cellularity, no crystals and sterile cultures.

Upon admission, imaging confirmed marked synovial thickening with minimal effusion as well as bone lysis. Synovial fluid Ziehl-Neelsen staining and, subsequently, cultures were positive for *Mycobacterium tuberculosis* and she was started on antituberculous quadritherapy.

Pancreatic NETs can be imaged using radiolabelled somatostatin analogues, such as ^{68}Ga-Dotatate PET/CT, since most express high levels of somatostatin receptors (SSTR). Peptide Receptor Radioligand Therapy with somatostatin analogues targeting SSTR2, such as ^{177}Lu-Dotatate, are recommended as second-line treatment.

Mycobacteria are contained in granulomas composed mainly of monocytes and lymphocytes, both of which express SSTRs. Clinically, this translates to radiolabelled somatostatin analogues' uptake in various granulomatous diseases, including tuberculosis and sarcoidosis.

Two hypotheses can be postulated for this patient's flares following each ^{177}Lu-Dotatate infusion. Firstly, SSTRs' activation by somatostatin analogues may also inhibit monocytes and lymphocytes through reduced phagocytosis and decreased IFN-gamma production respectively, leading to compromised anti-bacterial immunity and thereby triggering the flare. Alternatively, ^{177}Lu-Dotatate may directly be toxic to immune granuloma cells expressing SSTRs, destroying them the same way it does tumour cells. This may have led to relative loss of mycobacteria containment after each infusion, followed by leucocyte recruitment with a subsequent clinical flare.

To our best knowledge, this is the first description of tuberculous arthritis flaring on ^{177}Lu-Dotatate treatment and imaged on ^{68}Ga-Dotatate PET/CT, thus offering some insight on possible physiopathologic mechanisms at the granuloma level.

Case 2

Unilateral abducens nerve palsy as a complication of axial involvement of SAPHO Syndrome: A case report

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We here report on a 33-year-old female patient with a history of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome first diagnosed in 2019. She initially presented with involvement of the thoracic and lumbal spine, arthritis and osteitis of the sternoclavicular joint, enthesitis, and palmoplantar psoriasis pustulosa. Her previous treatments included NSAIDs, certolizumab (stopped because of worsening of psoriatic skin lesions) and prednisone. In September 2021, she presented with acute diplopia due to an incomplete right abducens nerve palsy. She also complained of a three months history of a progressive right sided headache. Laboratory analysis revealed elevated inflammatory parameters (CRP 28 mg/l, BSR 27 mm/h) without leucocytosis (10 G/l). A slight mononuclear pleocytosis with positive oligoclonal bands as well as intrathecal IgM and IgG synthesis were detected in the cerebrospinal fluid (CSF). A cranial MRI did not reveal cerebral lesions and an inflammatory CNS disease was therefore considered unlikely. However, MRI revealed osteitis of the clivus and the right basal part of the os occipitalis, surrounded by a pachymeningeal mass involving the middle cranial fossa. A PET-CT did not show evidence of lymphoma, malignoma or osteomyelitis. Whole body MRI revealed inflammatory lesions of the clivus, the cervical, thoracic and lumbar spine and of the manubrium. Prednisone at 1 mg/kg body weight was started and lead to resolution of diplopia within few days. In addition, she was given upadacitinib (15 mg/day) while prednisone was tapered to 5 mg/day over 10 weeks. A cranial MRI after 6 months revealed resolution of the osteitis in the clivus and occipital bone and regression of the pachymeningeal inflammatory mass. Clinical improvement and resolution of pain and morning stiffness were noted and the BASDAI declined from 6.2 to 3.3. ESR and CRP normalized.

In summary, we describe osteitis of the clivus, the occipital bone and pachymengeal inflammatory tissue that lead to a unilateral abducens nerve palsy as a manifestation of a preexisting SAPHO syndrome. Resolution of clinical symptoms, inflammatory markers and MRI lesions occurred under prednisone and upadacitinib.

Case 3

Successful treatment of refractory SLE-associated autoimmune hemolytic anemia with a low dose regimen using the CD38 directed monoclonal antibody daratumumab

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Autoantibody-secreting plasma cells seem attractive targets in patients with refractory SLE as suggested by preclinical models and clinical studies with proteasome inhibitors. More recently, the successful use of the CD38 directed monoclonal antibody daratumumab (16 mg/kg once weekly for 4 weeks) was reported in two patients with refractory SLE.1

Here we report on a 74-year old female patient who had been diagnosed with SLE in 2004 with Coombs-positive hemolytic anemia (AIHA), thrombopenia, mucocutaneous manifestations, arthralgias and lupus nephritis (WHO class IV) in 2006. She was treated with hydroxychloroquine, azathioprine, and cyclophosphamide until 2008 when mycophenolate mofetil (MMF) was started. During the following years, she developed a low-grade B-cell lymphoma where a watch-and-wait strategy was applied, a squamous cancer of the anus and vulva and of the lower lip where she received surgical and radiation therapy. As AIHA and nephritis were in remission, MMF was stopped in 2018 and the patient continued on hydroxychloroquine. Between January 2019 and April 2022 several relapses of AIHA occurred and were managed with high-dose methylprednisone and rituximab but the disease course was complicated by a septic jugular vein thrombosis and a recurrent late-onset severe neutropenia presumably related to rituximab that lead to mandibular

osteomyelitis. Systemic antibiotic treatment and filgrastim were initiated. Another hemolytic episode occurred in May 2021 when the patient received another course of rituximab but hemolysis reoccurred few months later. Stabilization was achieved by high-dose intravenous immunoglobulins and prednisone could be reduced to below 10mg daily. In April 2022, another hemolytic crisis occurred but the patient was refractory to high-dose steroids and intravenous immunoglobulins. No evidence for recurrence of lymphoma or any of the other malignancies was noted.

Daratumumab at 4mg/kg body weight was well tolerated with usual pre-medication. Subsequently, the dose was increased to 8mg/kg. Before the second infusion, haptoglobin had normalized and Hb increased from 63 g/l to 98 g/l and has stabilized since then. Thus far, the patient has received four infusions of daratumumab without any side effects.

In summary, low-dose daratumumab was successfully used in a patient with SLE and recurrent refractory AIHA but longterm efficacy needs to be confirmed.

1 Ostendorf L et al, N Engl J Med 2020;383:1149

Case 4

Severe acquired hemophilia as a complication of anti-TNF therapy responding to high dose prednisone, rituximab and the bispecific antibody emicizumab

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Autoimmune disorders including vasculitis, lupus-like syndromes, CNS demyelination and few cases of acquired hemophilia A characterised by autoantibodies against FVIII have been described as rare but relevant complications associated with anti-TNF therapies.

We here report on a 70-year old female patient diagnosed with antisynthetase syndrome in 2003, initially presenting with interstitial lung involvement, myositis and erosive arthritis. During the subsequent years, polyarthritis evolved as the dominant clinical manifestation. Previous therapies included cyclophosphamide, methotrexate, etanercept, abatacept and rituximab. Since 2016, the patient was in remission under certolizumab combined with leflunomide but in March 2020 developed pneumonia complicated by an in-hospital cardiac arrest and atrial fibrillation. Certolizumab was first discontinued but restarted in October 2021 when active synovitis relapsed.

The patient presented at the emergency room in March 2022 with extensive bruises and bleeding into the left iliopsoas muscle. A decrease in hemoglobin (Hb 63 g/l) and aPTT prolongation (154 sec) was detected. The suspected diagnosis of acquired hemophilia was confirmed by non-detectable FVIII (<0.01) and a high FVIII inhibitor titer (704 BU/ml). Certolizumab and leflunomide were discontinued. High-dose prednisone and rituximab (375 mg/m2 weekly over 4 weeks) were initiated. The patient was treated with recombinant FVIIa for 5 days that lead to resolution of bleeding. Four days later, the patient noted pain in the gluteal muscles with a decrease of hemoglobin (53 g/l) . A CT scan revealed extensive bleeding into the gluteal muscles and in both thighs. Recombinant FVIIa was restarted and, as levels of anti-FVIII antibodies were continuously high, treatment with emicizumab, a humanized anti-FIXa/FX bispecific antibody with FVIII mimetic activity was initiated at 3 mg/kg subcutaneously, weekly for 3 doses, followed by 1.5 mg/kg every 3 weeks. Within 3 days of the first dose, bleeding improved and hemoglobin increased. Five weeks later, FVIII inhibitor titer dropped to 90 BU/ml and an endogenous FVIII level of 16% was measured.

We present this case as an example of a rare and severe complication of a TNF inhibitor that was successfully treated with emicizumab, a bispecific antibody that replaces the hemostatic function of activated FVIII by bridging activated factor IX and factor X to activate factor X and allow the coagulation cascade to continue.

Case 5

Just a flue with heart failure

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In January 2022 we treated two young patients (26y & 37y) that were admitted to hospital because of fever and flu-like symptoms (Respiratory symptoms resp. abdominal symptoms). Due to a septic condition with significantly elevated inflammatory blood values (CRP 389mg/L, resp. 270mg/L) and pneumonic infiltrate, they were hospitalised and an antibiotic therapy was initiated. Shortly after admission, they became increasingly hemodynamic instable and were transferred to the intensive care unit with a catecholamine and oxygen dependency, severely decreased ejection fraction (20% resp. 40%), pericardial and pleural effusions and highly elevated cardiac markers (Trop-T: 2406ng/L, resp. 1874ng/L / NT-proBNP: 17805pg/mL, resp. 14976pg/mL). All blood cultures, Ag-tests, immune serologies were negative, but the patients were suffering from a cardiogenic shock with SIRS. Only a COVID-infection (mild symptoms resp. asymptomatic, PCR tested in 12/2021) three to four weeks past was remarkable in their health history. They received one resp. no vaccination before infection. Therefore the heart failure was interpreted as a myocarditis and the symptom complex as Multisystem Inflammatory Syndrome in Adults (MIS-A). The following days, they were treated with high-dose steroids (500mg resp. 250mg) at first, to which they responded well combined with catecholamines and inotrops. After a continued improving heart and infection blood work a slowly tapering regimen of the steroid therapy (down to 1mg/kg KG) and an IVIG therapy (2g/kg KG) for five days was initiated. The echocardiographic monitoring showed a positive development with a regression of the pericardial effusion and a normal cardiac output. With an improving general condition, the patients were discharged to either cardiac rehabilitation or home. A cardio MRT showed typical findings of a peri-/myocarditis with epicardial late-gadolinum enhancement (LGE) and in one patient additionally with myocardial LGE and edema.

The intention of this case series is to report on the rare but potentially lethal MIS-A, especially in a younger age group, predominant male after COVID-infection. Prompt recognition of MIS-A with immunomodulatory treatment is necessary to limit the hyperinflammatory response.

In the reported cases, it was especially remarkable that the patients underwent a mild initial infection and after a latency of several weeks a rapidly progressive reaction of immune disorder occurred.

Case 6

An enigmatic case of polyarthralgias

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Multicentric reticulohistiocytosis (MRH) is a rare multisystemic non-Langerhans cell histiocytosis characterized by skin and articular lesions and is often associated with cancer and other autoimmune disorders.

We report the case of a 50-year-old male that presented with diffuse inflammatory joint pain, exanthema on sun exposed areas and skin nodules on the face and hands, in the last 6 months.

The investigations showed high ANA titer (1:640), positive anti-ENA with specificity for anti-SSA and anti-SSB, positive RF (160 kUI/L). ESR, CRP and anti-CCP were negative.

There was no complement consumption, no monoclonal gammopathy and no cryoglobulins. The blood smear was normal. No proteinuria nor hematuria was found. Infection was ruled out, especially viral hepatitis, EBV,CMV, HIV, N. gonorrhoeae, C. trachomatis and M. tuberculosis. Schirmer's test was pathological but sialometry normal. Minor salivary gland biopsy was not significant.

Radiographs showed early signs of erosive arthritis on MCP and PPI. The PET CT revealed high uptake of large joints. A cranio-cervical MRI showed multiples nodules merging in bumpy cobblestone-like masses on the mucosa of the upper respiratory tract. Arthrocentesis of the right knee showed a sterile inflammatory synovial fluid without crystal.

Skin nodules biopsies identified a large histiocytic infiltrate occupying the superficial and middle dermis, composed of large cells with a finely granular eosinophilic cytoplasm, resembling ground glass. The immunohistochemistry was positive for CD163 and CD68 markers, but S100 protein was negative. Genome sequencing found no mutation in a large panel of genes, including BRAF, KRAS, MAP2K1 and NRAS.

The diagnosis of MRH with Sjögren's syndrome was established, according to ACR-EULAR2016 criteria.

Systemic workup for malignancy was negative, but investigation of other organ involvement revealed a central adrenal insufficiency without abnormality on cerebral MRI, except for a left parietal meningioma.

In accordance with the few case reports in the medical literature, our patient was treated with steroids, Methotrexate and Adalimumab.

Cutaneous and articular manifestations of MRH can be easily mistaken for dermatomyositis. As MRH can be associated to connectivitis, there is a high risk of delayed diagnosis. Biopsy of the cutaneous lesions is a key element in the diagnosis algorithm. As there is no standard treatment for MRH, a multidisciplinary approach is highly valuable.

Case 7

Bilateral adhesive capsulitis in a patient treated with isoniazid

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Adhesive capsulitis is a clinical diagnosis. In about 10% of cases, the damage is bilateral with a delay of a few months. We present here such a case in a context of isoniazid treatment accompanied by a speckled demineralization of both humeral heads.

A woman born in 1968 is known for cutaneous lupus confirmed by biopsy in 2012 and treated with hydroxychloroquine. Eye dryness with anti-SSA antibody raised the question of a possible Sjögren's disease. In 2018, she was treated by minimal surgery, radiotherapy and then hormone therapy (tamoxifen then anti-aromatase) for breast cancer. In April 2020, she was treated with Isoniazid for latent tuberculosis after a contact with an infected person. A few months later, both shoulders, elbows, wrists and fingers become painful with functional limitation. On clinical examination, the mobility of the shoulders is strongly limited in all ranges of motion. Absence of peripheral synovitis. Biologically, there is a moderate elevation of the sedimentation rate (28). CRP is normal. X-rays of both shoulders show a speckled demineralization of the 2 humeral heads. The scintigraphy shows moderate inflammatory activity in the acromioclavicular and glenohumeral joints. In view of the clinical picture and the radiographs, the diagnosis of bilateral frozen shoulder is retained.

In this patient, the question of systemic arthritic involvement arose in view of the chronic cutaneous lupus and possible Sjögren's disease. However, the clinical approach allowed to rule out this hypothesis and to retain a bilateral adhesive capsulitis of the shoulders. Breast surgery was probably not involved (minimal surgery, 18-month delay between surgery and onset of pain). The hypothesis of a fibrosing arthropathy due to isoniazid treatment is supported by the chronology of the facts, by the bilaterality and by the extension of the phenomenon, notably to the elbow, the wrist and the fingers of the right side. Several case series of shoulder-arm syndrome after isoniazid were reported in the 1960s. The origin remains unknown although several physiopathological hypotheses have been reported.

This case illustrates the resurgence of side effects of anti-tuberculosis drugs that have been forgotten since tuberculosis was restricted to risk groups. Routine check-ups before starting modern therapies frequently lead to the detection of latent tuberculosis and to the wider use of these old products.

Case 8

Two birds with one stone – Rituximab in a patient with rheumatoid arthritis and microscopic polyangiitis

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A combined onset of rheumatoid arthritis (RA) and microscopic polyangiitis (MPA) is possible but rare; less than 50 cases have been described in the literature. However, with rituximab, we have an effective treatment available tackling both diseases at once.

A 43-year-old man was referred by his family doctor for joint complaints and acute renal insufficiency with proteinuria.

The patient reported inflammatory joint pain and swelling in the hands and feet with associated morning stiffness for 2-3 weeks. Other complaints suggestive of a systemic autoimmune disease were absent. Clinical examination revealed symmetric polyarthritis of the hands and feet and arthritis of the right knee. Synovial fluid analysis of the right knee showed an elevated cell count of 3300

cells/ul with no evidence of crystals or bacterial growth. No degenerative or post-inflammatory changes were seen in conventional radiographs of the involved joints. Further testing revealed a normochromic normocytic anemia (Hb 13.5 g/dl), an elevated CRP (55 mg/l), elevated creatinine (164 umol/l, eGFR = 44ml/min), positive rheumatoid factor (127 IU/ml) and positive anti-CCP antibodies (>340 E/ml). Based on the clinical and serological findings, diagnosis of RA was made.

Further workup for renal insufficiency revealed a nephritic urine sediment with proteinuria and dysmorphic erythrocytes, positive ANCA (1:320) and positive anti-MPO (47 U/ml) antibodies in additional serologic tests. Subsequently, a kidney biopsy was performed, showing a focal global and segmental sclerotic and focal-extracapillary proliferating and necrotizing pauci-immune glomerulonephritis. Together with the clinic and laboratory analysis, these biopsy findings led to the diagnosis of MPA with primary kidney involvement.

Immediate therapy with intravenous methylprednisolone (500mg/d for 3 days) and rituximab (750mg, followed by 4 x 375mg/m2) was initiated to treat and stop progression of MPA associated renal failure. Renal function and proteinuria responded excellently, allowing oralization of cortisone therapy with tapering over time. Not surprisingly, this therapy also resulted in significant improvement of joint symptoms.

This case impressively shows that the presence of one autoimmune disease does not exclude the occurrence of a second - unrelated autoimmune disease. Fortunately, with a B-cell depleting approach, it is therapeutically possible to treat both ANCA-associated vasculitis and RA simultaneously - with one stone.

Case 9

CPPD omarthritis with osteonecrosis in a young patient with sickle cell crisis – a case report

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Sickle cell crisis can lead to acute musculoskeletal pain related to vaso-occlusion and tissue infarction including peripheral joints.

Appropriate management may be challenging especially in the context of avascular necrosis.

We here report on a 23-year old male patient from Angola who presented with acute right-sided shoulder pain with a frozen-shoulder like limitation of movement during an acute haemolytic crisis. Sonographic evaluation confirmed omarthritis with a bulky glenohumeral effusion. Sonographically guided arthrocentesis showed an impressive number of leucocytes in the synovial fluid (132 G/l, 98% neutrophils, 20ml) and calcium-pyrophosphate crystals. MRI demonstrated infarction of the humerus head with concomitant synovitis. Short-term NSAID were prescribed, instead of systemic or intraarticular steroids in view of the MRI-proven osteonecrosis. The patient recovered within two weeks.

Case reports have described coexisting gout in joints affected during sickle-cell crisis. However, to our knowledge, this is the first case describing a patient suffering from concomitant CPPD omarthritis in the context of avascular necrosis, with glenohumeral synovitis during sickle cell crisis. We hypothesize calcium pyrophosphate release associated with or originating from the osteonecrotic lesions of the humerus head.

This case report underlines the importance of rheumatologic evaluation and arthrocentesis in patients with acute arthritis during sickle cell crisis to allow a definite diagnosis and to optimize management.

Case 10

A case of rhupus and spondylarthritis

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We report the case of a 76-year-old woman, who presented with a 2-year history of polyarticular joint pain (MCPs, PIPs, wrists, shoulders, hips, knees, ankles) with morning stiffness, associated with fatigue, night sweats, weight loss, headache and cough. Since 2013, she reported a facial rash on sun exposure. In addition, she described low back pain relieved by NSAIDs. The clinical examination revealed a left knee effusion without other arthritis. Synovial fluid aspiration of the left knee was inflammatory, and rare calcium pyrophosphate crystals were observed. Laboratory tests showed elevated ESR and CRP, high ANA titer, anti-CCP and anti-dsDNA positivity.Anti-phospholipids and rheumatoid factor were negative.There was no complement consumption, no monoclonal gammopathy, proteinuria, or haematuria. X-rays showed hand osteoarthritis, chondrocalcinosis of knee meniscus and pelvic symphysis and erosion of the left third MTP suggestive of rheumatoid arthritis. A diagnosis of overlap syndrome with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) (rhupus) was made.A component of CPPD-related arthritis was also suspected. Treatment with glucocorticoids and hydroxychloroquine (HCQ) was initiated. After glucocorticoid tapering, methotrexate (MTX) was started due to persisting symptoms and inflammation.After 6 months of treatment, the patient was hospitalised for increased back pain. Spinal MRI revealed inflammatory changes in the thoracic spine and both sacroiliac joints, suggestive of spondylarthritis (SpA). Blood tests showed marked inflammation, and HLA-B27 was negative. We retained the additional diagnosis of axial spondylarthritis. The combined treatment of MTX and HCQ was continued, and back pain was well controlled with NSAIDs. We report here a concurrent diagnosis of SLE, RA and SpA. The coexistence of RA and SLE is well known, but the coexistence with spondylarthritis has only been rarely reported. Shared genetic risk factors may contribute to this phenotype. In conclusion, this clinical scenario is challenging in terms of diagnosis, as RA and SpA are generally mutually exclusively considered. However, the rheumatologist should bear in mind that they can rarely coincide.The choice of treatment is also problematic to treat all the inflammatory conditions. JAK inhibitors were considered, being effective in RA and SpA and preferred to anti-TNF owing to SLE,but were not needed for the moment as the conditions were relatively well controlled.

Case 11

New-onset Idiopathic inflammatory myopathies during pregnancy: a case series

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Idiopathic inflammatory myopathies (IIM) are rarely described with new-onset during pregnancy. In reported cases of IIM that developed during pregnancy, the outcome of pregnancy is often poor. We here report two current cases followed at our department.

Case 1: A 28- year-old woman had been complaining about arthralgia, myalgia and Raynaud's when she became pregnant in September 2021. Her physical examination revealed mechanic's hands and weakness of proximal muscle groups. Diagnostic tests revealed elevated muscle enzymes (CK 3248 U/l (<170), CK-MB 59.4 U/l (<3.6), Trop T-hs 111.2 ng/l (<14)), a highly positive ANA (1:1280) and positive anti-PM-Scl 100. MRI showed myositis that was verified by muscle biopsy. Anti-PM-Scl 100 Myositis could be diagnosed. Therapy

with prednisolone 60 mg/day was promptly started. By gestational week 10, she was admitted due to tetraparesis, respiratory muscle weakness (FVC, FEV1 by 55%), dysphagia and dysphonia. Pulse i.v. methylprednisolone followed by oral prednisolone, IVIG and azathioprine were initiated. Despite of parenteral nutrition, she developed an aspiration pneumonia. In addition, cardiac MRI revealed myocardial involvement.

Case 2: A 38-year-old woman with a history of smoking and hypovitaminosis D became pregnant in December 2021. During her first trimester, she developed a photosensitive rash on her forehead, myalgia, a proximal muscle weakness, peripheral oedema, erythema nodosum. Muscle enzymes were markedly elevated (CK 3658 U/l, CK-MB 19, with positive ANA 1:320 and positive anti-NXP2 antibodies. MRI showed necrosis of muscle fibre, inflammation and subcutaneous fascial oedema. Anti-NXP2 Dermatomyositis was diagnosed. An underlying malignancy could be excluded. Pulse i.v. methylprednisolone followed by oral prednisolone, IVIG and azathioprine was started. During three months of persistent disease activity, she developed tetraparesis, dysphagia, myocarditis, an ulcerating erythema nodosum and calcinosis. A treatment escalation with RTX was necessary and cyclosporine A and hydroxychloroquine were added to azathioprine and prednisolone.

In both cases, disease remission could be achieved after 3-4 months using a pregnancy-compatible extensive combination therapy. In the ongoing pregnancies, there were no signs of preeclampsia or gestational diabetes. During active disease, prenatal ultrasound screenings showed signs of fetal growth restriction that resolved after effective disease control.

Case 12

A case of adult-onset chronic recurrent multifocal osteomyelitis treated with anti-TNF agent

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We report the case of a 29-year-old woman hospitalized initially in October 2021 for a two- week history of multiple joint pain (feet, ankles, knees) and constitutional symptoms (night sweats, low-grade fever of 38°C). There were no cutaneous, respiratory or digestive symptoms. Both ankles and the left knee were warm without swelling on physical examination and were painful on palpation, especially bony protuberances.

The investigations showed elevated inflammatory markers (CRP 101 mg/L, ESR 54 mm/h) without auto-immunity (rheumatoid factor, anti-CCP and ANA were negative). HLA B27 was absent. Low vitamin D levels were observed, and LDH and β2 microglobulin were slightly increased. An MRI of the lower limbs completed with a total body MRI revealed the presence of multiple bone oedemas (hyper T2 lesions) with a metaphyseal distribution without axial involvement. Thus, the initial diagnosis of transient osteoporosis was revised for a chronic recurrent multifocal osteomyelitis (CRMO). Differential diagnoses comprised: sarcoidosis, osteocytosis, Still's disease and lymphoma.

Due to the atypical clinical and radiological presentation, a bone biopsy of the femoral diaphysis was performed that excluded a neoplastic condition.

During follow-up, MRIs were performed regularly and showed the migration of T2 lesions, with the disappearance of the lesions initially observed and the appearance of new lesions affecting diaphysis and epiphysis in T2 hypersignal, suggestive of CRMO.

In terms of treatment, NSAIDs showed no efficacy in treating pain, and the patient received an infusion of zoledronic acid (5 mg) that allowed a significant decrease in pain. However, the patient presented a relapse three months later. Thus, NSAIDs were started again and combined with high dose glucocorticoids (0.7 mg/kg). Due to limited efficacy, we started an anti-TNF agent (adalimumab), initially combined with Methotrexate that could be stopped after that. The patient reported a significant pain reduction under monotherapy with adalimumab at the last visit.

In conclusion, we report a case of CRMO beginning in adulthood, while this condition usually affects children. The patient presented numerous bone lesions on MRI and severe pain that could only be controlled with an anti-TNF agent.

Case 13

Large-vessel vasculitis and hearing loss as clinical presentation of Cogan syndrome

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Cogan Syndrome is a rare disorder. It is defined according to David G. Cogan by coexistence of non-syphilitic interstitial keratitis and audiovestibular symptoms occurring less than 2 years apart.

A 47-year-old woman presented to our otorhinolaryngology (ORL) department with a history of slowly progressing hearing loss over 8 years and vertigo. In addition, she described a history of keratouveitis. Tone audiogram initially showed significant sensorineural hearing loss of 76% (right side) and 79% (left side). Cogan syndrome was suspected after earlier ORL consultations abroad, but further diagnostic workup was not done, and no treatment was initiated.

One year later, she was referred to our hospital because of progress in hearing loss to 87% and 100 % respectively. A short course of glucocorticoids did not improve hearing loss.

In addition to the history already taken by the ORL and ophthalmology departments, the patient complained about abdominal pain and severe fatigue for the last 6 months. Laboratory workup showed elevated inflammation markers (CRP 31 mg/l; normal: <8 mg/l, BSR 52 mm/h; normal: <12 mm/h) while no specific autoantibodies were present (ACPA, Rheumatoid factor, ANCA, ANA,). The following PET-CT examination showed active vasculitis of the thoracic aorta, the supraaortal vessels, the infrarenal aorta and the left arteria iliaca, compatible with large-vessel vasculitis.

We started treatment with prednisone 1 mg/kg and added infliximab 4 mg/kg, initially at intervals of 4 weeks. The clinical symptoms of abdominal pain and fatigue improved dramatically. Interestingly, tone audiometry remained stable after 5 months of therapy but showed slight improvement after 1 year of therapy. MRI of the aorta and its branches showed no signs of active inflammation after 5 months and 1 year of therapy.

The patient suffered from non-syphilitic interstitial keratitis, audiovestibular symptoms and described an interval between the manifestations of less than 2 years. Cogan's original criteria were therefore retrospectively fulfilled. Prevalence of Cogan syndrome is unknown, about 300 cases have been reported so far. Vasculitis in vessels of variable size may occur, as mentioned in the 2012 Chapel Hill Consensus Conference. Aortitis is estimated to be present in 10%. Data regarding therapeutic options is scarce. The best clinical outcomes have been reported when glucocorticoids were combined with infliximab, which is why we opted for this combination therapy.

Case 14

A young patient with skin exanthema and progressive central nervous deficits.

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In October 2020, 19-year old patient presented to our hospital with left-sided swelling and pain of the mandibular joint as well as double images and hearing loss on the left ear since one month. Upon presentation, several psoriasis-like skin lesions were observed at arms and forearms, no pustulosis could be found. CT imaging revealed erosive osteitis and osteomyelitis as well as hyperostosis and periost activation of the left mandibular joint. In addition, inflammatory changes at the base of the skull with narrowing of the canalis caroticus with compression of Nn. Abducens and vestibulocochlearis were noted. No other signs of osteitis or hyperostosis could be found on whole body MRI.

Opthalmologic assessment revealed myopia and palsy of the left M. abducens. In addition, a sensorinneural hearing loss of 61% was detected.

Biopsies of the left mandibular bone showed chronic, partly granulomatous inflammation without evidence of infection. NSAIDs treatment led to improvement of local swelling, inflammatory markers and disappearance of double images, whereas hearing loss remained unchanged. A second biopsy eventually showed growth of Streptococcus and Actinomyces species, antibiotic treatment was initiated and NSAR were stopped. Hereafter left-sided mandibular swelling and inflammatory markers raised again. NSAIDs were restarted with good effects on swelling and inflammatory markers.

In January 2021 the patient presented with motor deficits of the left-sided mimic muscles as well as incomplete closure of the left eye lid. MRI revelaed pachymeningitis involving the meatus acusticus internus on the left, as well as the N. mandibularis, the N. petrosus major and N. facialis. Liquor analysis revealed no signs of infection, i.v. Solumedrol treatment was started, which led to partial recovery from facialis palsy.

Taken together we concluded that SAPHO syndrome with central nervous complications (partly inflammatory, partly mechanical) as the most probable diagnosis. Under therapy with infliximab the patient improved constanly and steroids could be tapered off. Unfortunately, in May 2022 the patient presented again with increasing signs of inflammation and reappearance of double images. Subsequently, a relapse of mandibular inflammation and pachymeningitis was found. Detection of anti-drug antibodies to infliximab suggested secondary loss of function of infliximab. Consequently, treatment with another, less immunogenic anti-TNF mAb was pursued.

Case 15

Otitis media and inflammatory tumors mistaken for infection and malignancy in ANCA-associated vasculitis

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Introduction: Otitis media, partial hearing impairment and facial nerve palsy are uncommon presentations of ANCA-associated vasculitis (AAV). We report the case of a patient with prolonged multiorgan inflammation including several spinal locations, mistaken for infectious and malignant lesions, finally diagnosed as AAV after months of unspecific treatment.

Patient and therapy: This otherwise healthy 68-years-old female presented with symptoms of upper airway infection and a bilateral otitis media unresponsive to various antibiotics. Three months later, she additionally developed facial nerve palsy and progressive bilateral hearing impairment. A glucocorticoid therapy for facial nerve palsy lead to remission of inflammation and nerve palsy, yet night-sweats, weight loss and anemia developed additionally. Suspicion of an underlying immunological disorder led to vasculitis work-up with high titres of PR3-positive c-ANCAs. A CT scan showed congested paranasal sinuses and tumoral structures in both upper pulmonary lobes not typical for granulomatous formation. An additional PET-CT revealed multiple metabolically active areas in the mastoid cells, middle ears, larynx, lungs, thoracic and lumbar spine – the latter being suspicious of either spondylodiscitis or tumour. Eight biopsies of most of the hot spots showed chronic, in part destructive inflammation yet cultures remained negative. Finally, the biopsy of the maxillary sinus showed histological findings consistent with GPA in 1 of 6 specimens. Oral glucocorticoid therapy (1 mg/kgKG) was initiated and remission induction was started using Rituximab with 1000 mg twice in a fortnightly interval.

Results: Three months after Rituximab, the patient is in good condition, experiencing complete remission of inflammation, anemia, normalization of PR3-ANCA and regression of thoracic, maxillary and spinal affections. Follow-up PET-CT showed remission of the metabolically active findings of the maxillary sinus and the spine, further indicating a good response to therapy. Yet there was no recovery of the hearing loss.

Conclusions: A first episode of otitis media in an adult person should always rise suspicion for vasculitis, especially AAV. Further vasculitis work-up should then be prompted in order to rapidly diagnose (or exclude) possible AAV and initiate remission-inducing therapy in order to avoid permanent organ damage.

Case 16

Is it arthritis or not? An unusual presentation of a chronic infection

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Introduction: Acrodermatitis chronica atrophicans is a late cutaneous manifestation of Lyme borreliosis and is predominantly located on the distal extremities. The progress over months to years is typically characterized by an edematous inflammation followed by a chronic atrophic state. We report a case of a patient with a painless swelling of the left hand and the diagnosis of Lyme borreliosis was made with a positive serology and PCR in the skin biopsy.

Patient and therapy: The patient, a 93-year-old-man, presented with a 5-year history of painless bluish-red swelling over the dorsal side of the left hand, particularly over the wrist and the forehand (picture A). His medical history was notable for a monoclonal B-cell lymphocytosis in the peripheral blood without cytopenia. Laboratory findings revealed no systemic inflammation. Infectious workup showed a positive serology for Borrelia with high level of immunoglobulin G. Ultrasound and radiographic examinations showed no synovitis nor bone erosions, respectively. Magnetic resonance tomography of the left hand revealed a diffuse edematous infiltration of the subcutaneous tissue and dermis with no signs of synovitis or bone marrow edema (picture B). To exclude a leukemic infiltration considering the patient`s history, we performed a punch biopsy of the skin. Histology showed a dense dermal lymphohistiocytic infiltration with no signs of lymphoma. Immunochemistry was negative for spirochete species, but PCR positive for Borrelia afzelii. Detailed history revealed an erythema migrans without antibiotic treatment about 8-years before, indicate early localized Lyme infection at that time. After a 4 week of antibiotic treatment with doxycycline 100 mg orally twice daily, we found a marked clinical improvement with little residual swelling of the left hand (picture C).

Conclusion: Acrodermatitis chronica atrophicans is a late manifestation of Lyme borreliosis and as its nomenclature, typically characterized by skin atrophy. We present a case with a persistent edematous skin and tissue inflammation even after 8-years of infection, representing the various clinical presentation of Lyme disease.

Case 17

A case of a tick-borne meningoencephalitis with a C5 radiculopathy developed lately

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Introduction: Here we report a case of a radiculitis after the acute/sub-acute phase of tick-borne meningo encephalitis (TBE).

Case presentation: A 64-year-old male in good general health was admitted to the emergency department complaining of fever, diffuse arthromyalgia, dizziness and impaired general condition. Lumbar punction results showed a hyperproteinarygia and lymphocyte pleiocytosis, although serology for flavivirus was not made because of sparse sample. However, positivity to flavivirus was observed in serology blood tests. The patient had recent history of tick bites. A diagnose of TBE was then made based also on clinical and radiological criteria.

12 days later the patient described the sudden appearance of an intense pain, on the posterior part of the right shoulder, associated with a decreased proximal muscle strength of right upper limb. Clinically he presented with an atrophy of infraspinatus and supraspinatus muscles, without deltoid muscle atrophy.

In the follow up, there was a slow progression in what concerns pain and mobility, especially during external rotational movements and maximum abduction of the shoulder.

Investigations and differential diagnosis: Magnetic resonance of the brachial plexus showed a T2 hypersignal contrast taking of the right infraspinatus and supraspinatus muscles evoking denervation lesions (in the territory of the right supraclavicular nerve).

A medullary magnetic resonance only showed moderate disc disease C5-C6 and C6-C7, without any spinal cord injury associated.

Results from an initial electroneuromyogram (ENMG) suggested motor neuropathy of the supraclavicular nerve (Sunderland stage 2-3) and the axillary nerve (Sunderland stage 2) presumably para-infectious in connection with TBE diagnosis.

Another ENMG was repeated 7 months later highlights arguments for a C5 radiculopathy (viral radiculitis) such as reinnervation of affected infraspinatus, supraspinatus, rhomboid, and deltoid muscles, without touching brachial biceps muscle (predominantly C6 innervation). It was also observed improvement and recovery in the amplitude of motor response of the axillary nerve. In addition, no sensory involvement was detected.

Conclusion: We present a case of TBE presenting with a C5 radiculopathy developed lately. Early diagnosis of neurological manifestations can lead to the introduction of early physiotherapy. In this patient, progression was seen but it persisted some pain and affected mobility months after.

Case 18

Case report: post-Covid-19 arthritis and peri arthritis

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We present the case of a 63 years old male patient known for type 2 diabetes and sleep apnoea. He was admitted as inpatient for a non-traumatic severe and disabling left hip pain. The pain started progressively one month ago. The medical history was otherwise irrelevant, with no general symptoms nor other symptoms suggestive of an inflammatory disease. To mention a history of an asymptomatic SARS-COV2 infection, diagnosed by a naso-pharyngial PCR, approximately 10 days before the onset of the pain.

On physical examination, the patient was afebrile. The palpation of the inguinal region was tender on palpation with marked limitation of the hip range of motion. The spine and other peripheral joints were painless without inflammatory sign. Moreover, there was no skin lesion nor inguinal lymph nods enlargement. Due to the importance of pain with marked functional limitation, the patient is hospitalized for investigations and pain-management.

On blood sample there was a mild increase of inflammatory markers (CRP 25mg/l, VS 20mm/h) with normal cell count. Standard X-rays of the pelvis and hip were normal. The MRI of the hip showed a mild coxo-femoral arthritis with marked inflammation of the surrounding musculature. An arthrocentesis was performed and 2ml of serous fluid was aspirated. There were no crystals. The cellularity could not be tested due to small amounts of fluid. The synovial culture showed a polymicrobious growth compatible with contamination.

In summary, we were facing a patient with an acute and very painful hip monoarthritis. There was no history of gastrointestinal or urinary tract infection, the search for C. trachomatis and N. gonorrhoea in urines was negative. An extensive serologic testing (HIV, HBV, HCV, HBV, HCV, HIV, Lyme, Syphilis, Coxiella, Bartonella, Brucella & Quantiferon) and the search for T. whipplei were negative as well. There was no HLA-B27 and rheumatoid factor, ACPA, ANA, ANCA and specific antibodies related to polymyositis were negative. The chest-abdomen-pelvis scan showed no sign of neoplasia. To rule out a vasculitis we proceeded to a PET-CT, which showed no sign of vasculitis or myositis.

Considering the timing of the onset of the symptoms and the absence of any other diagnosis, the patient was diagnosed with reactive arthritis caused by SARS-COV2. The patient was treated with Diclofenac 150 mg/day and opioids. The clinical evaluation one month after discharge showed a spontaneous significant improvement

HPR

HPR 1

Interprofessionelle Zusammenarbeit - Studierende der Klinik für Rheumatologie am USZ üben für die Zukunft. Ein Erfolgsprojekt aus der Praxis

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Studierende der Professionen Medizin, Physiotherapie, Ergotherapie, Pflege und Ernährungsberatung tauschen sich in der interprofessionellen Fallbesprechung (IPF) auf Augenhöhe aus und erwerben dabei wichtige Kompetenzen. Die Sicht auf die Patientin/den Patienten vervollständigt sich und sie/er profitiert von einem abgestimmten Behandlungsplan.

Ausgangslage: Der Transfer theoretisch erworbener interprofessioneller Kompetenzen in den klinischen Alltag ist zentral und wird von Experten gefordert. Nur durch Bildungsangebote in der realen Berufspraxis können Studierende effektiv auf die aktuellen und kommenden Herausforderungen der Gesundheitsversorgung vorbereitet werden.

Die Bildung Physiotherapie Ergotherapie Universitätsspital Zürich entwickelte das Konzept der IPF für Studierende. Dieses wurde auf der Klinik für Rheumatologie 2019 pilotiert und wird seither regelmässig erfolgreich umgesetzt (Caduff et al., 2021).

Konzept der «Interprofessionellen Fallbesprechung für Studierende»: Die IPF besteht aus mehreren Lerneinheiten, welche am selben Tag geplant werden. Das Konzept beinhaltet die folgenden Elemente:

- Auswahl einer/s sich aktuell auf der Klinik befindenden Patientin/Patienten
- Monoprofessionelle Patientendarstellung (in Stichworten, nach Vorlage)
- Patientengespräch
- Interprofessionelle Fallbesprechung: Nach einem vorgegebenen Schema besprechen die Studierenden mit Hilfe einer/eines Moderatorin/Moderators die/den Patientin/Patienten. Das Resultat ist eine interprofessionelle Patientendarstellung, ein gemeinsames Verständnis der Patientensituation sowie ein interprofessioneller Behandlungsplan.
- Rückmeldung an die/den Patientin/Patienten
- Reflexion (schriftlich)

Zielsetzung: Die Studierenden erwerben interprofessionelle Kompetenzen in den Bereichen:

- Teamfähigkeit/Wertschätzung
- Lernen im interprofessionellen Team
- Erläutern von Professionsspezifische Sichtweisen
- Kommunikation
- Offenheit/Flexibilität

Ergebnis und Nutzen: Die IPF wird durch die Studierenden als sehr nützlich hinsichtlich des Erwerbs von interprofessionellen Kompetenzen evaluiert. Berufsbildende erweitern durch die Herausforderung der Moderation ihren Horizont. Patientinnen und Patienten profitieren von einem optimierten Behandlungsplan, der von allen Professionen anerkannt und umgesetzt wird.

Posterpräsentation: Am Kongress wird das Konzept vorgestellt. Zudem wird anhand eines Patientenbeispiels der IPF auf der Klinik für Rheumatologie der Nutzen verbesserter interprofessioneller Zusammenarbeit dargestellt.

HPR 2

Revision of a Patient-Specific Work-Tool including Feedback from all Stakeholders for the Bern Ambulatory Interprofessional Rehabilitation Program (BAI-Reha) for Patients with Chronic Musculoskeletal Pain

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Background: The Bern Ambulatory Interprofessional Rehabilitation Program (BAI-Reha) is a 12-weeks-program for patients with chronic musculoskeletal pain aiming at return to work and improving quality of life. The Patient-Specific Work-Tool for the BAI-Reha exists since 2017. We developed the Work-Tool as a folder with lots of information and worksheets to be used during and after the BAI-Reha. Nevertheless, we realized over the years, that it was never quite used as planned.

Aim: To adapt the Patient-Specific Work-Tool so that patients and staff use it more regularly.

Methods: The adaptation-process included feedback and peer-reviews from all stakeholders: patients of the BAI-Reha, all members of the professional team (physio- and occupational therapists, psychologists, social workers, physicians and nurses). Feedback targeted content and structure, daily use and physical presentation of the Work-Tool. For this, we conducted single interviews and focus groups. We evaluated a specific text concerning "Pain Education" directly with patients for comprehensibility and applicability, twice.

Results: The Work-Tool and its index are now lighter and clearer and give a better overview for all stakeholders. Worksheets are actively distributed when used, not included as a fixed content of the folder. We established a new interprofessional sheet as an overview for home-exercises. The text concerning "Pain Education" was adapted. We integrated new content such as follow-up services, and recommendations for apps and books.

Conclusion: All stakeholders were satisfied with the involvement in the adaptation-process and now use the Work-Tool more actively. We have already planned to re-evaluate the Work-Tool after six months in use.

HPR 3

Case Management - effizient und personenorientiert

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Langwierige diagnostische Abklärungen, mehrfache fachärztliche Konsile und vielfache Untersuchungen – bis eine Diagnose feststeht, kann viel Zeit vergehen. Insbesondere für PatientInnen mit akuten Schmerzen in einer komplexen Problemlage.

Hier sind einerseits Kriterien gefragt, die Betroffene frühzeitig in ein Case-Management einschliessen, andererseits Fachexpertise und Beratungskompetenz die das Selbstmanagement fördern und den Behandlungsprozess effizient personenorientiert steuern.

Hintergrund: Aufgrund akuter Schmerzzustände im Bereich der Wirbelsäule kommt es bei chronisch erkrankten Menschen immer wieder zu kurzfristigen stationären Aufnahmen in die Klinik für Rheumatologie. Die PatientInnen sind mit einer plötzlich eintretenden hohen Schmerzintensität und funktionalen Beeinträchtigungen konfrontiert, deren Ursache vorerst unklar ist. Das ist für die Betroffenen und ihre Angehörigen herausfordernd und hat auch ökonomische Folgen. Im Jahr 2018 führte dies zu einem erheblichen Defizit im

sechsstelligen Bereich. Dies veranlasste die Klinikleitung, ein durch die Pflegeexpertin geleitetes Case Management zu entwickeln, um komplexe Aufnahmesituationen mit hohem interdisziplinären Koordinationsbedarf zu optimieren.

Methode: Um sicherzustellen, dass das Case Management Handlungskonzept in die betrieblichen Rahmenbedingungen eingebettet ist und die bestmögliche Wirkung erzielen kann, orientierten wie uns an den Prinzipien des Chance Management Prozesses. Eine interdisziplinäre Projektgruppe mit der Pflegeexpertin, einem Oberarzt und der Abteilungsleitung haben ein Handlungskonzept erstellt sowie Intake Kriterien entwickelt, welche den Cut-off-point für den Einschluss in ein Case Management bildeten. Die Ziele waren die Zielverweildauer bei dieser Patientengruppe um durchschnittlich 2-5 Tage zu reduzieren und die Qualität und Effizienz der Behandlung durch die Abstimmung auf die Bedürfnisse der betreuten Personen zu steigern.

Ergebnisse: Während der siebenmonatigen Projektphase wurden insgesamt 64 Personen der Zielgruppe ins Case Management aufgenommen. Die Überschreitung der Verweildauer betrug durchschnittlich 1.03 Tage. Der zeitliche Aufwand für Case Management Tätigkeiten belief sich zwischen 5 und 36 Minuten. Dabei generierte die Altersgruppe der unter 61-jährigen, wenn zusätzlich noch eine psychiatrische Nebendiagnose und/oder komplexe Schmerzzustände vorlagen, den höchsten Zeitaufwand. Die Case Managerin konnte in Zusammenarbeit mit allen Beteiligten das Entlassungsmanagement optimieren und zur Prozessabstimmung der Patient*innen beitragen.

Schlussfolgerungen: Die Ergebnisse unserer Evaluation zeigen, dass Case Management unter der Leitung einer Pflegeexpertin sich in hohem Masse eignet, um die Qualität und Effizienz bei der Betreuung der Zielgruppe zu erhöhen. Dies belegt die eindrückliche Reduktion der Verweildauer und die Zufriedenheit des Behandlungsteams.

HPR 4

Difference in muscle force ratio of trunk flexors and extensors in healthy subjects and people suffering from low back pain: A meta-analysis

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Background: In Switzerland, two out of five people suffer from low back pain (LBP). In 85% of LBP cases, the pain is considered non-specific.

Objective: The aim of this systematic review was to synthesize findings from studies analyzing the ratio of peak torque of trunk flexor and extensor muscles in the context of non-specific LBP.

Method: An initial literature search was undertaken on PubMed and Cochrane databases. Relevant studies were extracted by two reviewers. The quality of each study was evaluated with the AXIS tool. The specific inclusion criteria stipulated that only studies having measured peak torque in an upright position by means of isokinetic dynamometer were included. No search restriction relating to age or gender quotas were implemented.

Results: A total of 3002 studies were identified by the initial database search of which 10 studies fitted the specific inclusion criteria of this systematic review. A total of 938 participants divided into two groups, (Group A (p = 232): participants with non-specific low back pain (LBP), group B (p = 751) participants without any low back pain (nLBP)) comprised the data for this systematic review.

The meta-analysis of the data showed a statistically significant difference within the nLBP group. The ratio of peak torque between trunk flexors and extensors in the nLPB group is less than 1 and implies that muscle groups contributing to trunk extension are stronger than those for flexion.

In the LBP group a statistically insignificant difference of the peak torque ratio between trunk flexors and extensors was established. The ratio for this group was 1.15. The results of this systematic review were considered to be statistically significant if the confidence interval did not intersect with the ratio at 1.

Whilst no statistically significant conclusion could be drawn for the LBP group, a trend towards weaker trunk extensors in comparison to trunk flexors was observed.

Conclusion: Isokinetic dynamometer measurements conducted in an upright position show that participants with nLBP have statistically significantly stronger trunk extensors compared to trunk flexors. There is a tendency for participants with LBP to have weaker trunk extensors than flexors. The imbalance between trunk flexors and extensors could be a contributing factor in the multifaceted causes or results of non-specific LBP.

Key words: Non-specific low back pain, strength ratio, peak torque, trunk, trunk flexion and extension, isokinetic dynamometer

HPR 5

Supporting Nurses to develop knowledge and skills to empower their young adult patients to self-manage their chronic conditions

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Promoting self-management skills in adolescents and young adults, is very important, in order to empower them to deal with their lives in a manner that suits them, but does not endanger their health. Adolescents and young adults with a chronic illness need support to develop the skills and knowledge to manage their illness.

In a joint initiative, two clinical nurse specialists from the young adult rheumatology clinics in the University Hospital Bern and Basel ran a workshop for nurses who work with adolescents and young adults across several chronic conditions. The focus of the workshop was to raise awareness amongst nurses of the concept of self-management and to introduce the skills to promote the topic amongst their patients.

The workshop ran online over two hours, enabling nurses from different hospitals, in two different cities to participate. The workshop was interactive, with the use of breakout rooms, and varied content including a quiz, theory input and video. The theoretical input explained the concept based on the chronic disease self-management platform published by the federal office of public health. This was followed by a video of a young patient, where she outlined her strategies for living with her illness and the challenges she has faced to date. The participants had an opportunity to discuss both these segments in small groups and then feedback their discussions to the bigger group. The discussions were prompted by questions provided by the organisers. There were regular short breaks built in to the programme to support the participant's active involvement.

Ten nurses participated from several different specialities and four different adult and paediatric hospitals. All the nurses work with adolescents or young adults in their clinics. Four nurses were unable to participate at the last moment due to the workload on their units and had to withdraw. The feedback from the nurses at the end of the session was positive. They appreciated the variation in the style of content and the combination of theory and practice. One nurse mentioned that she preferred face-to-face learning but most of the nurses were satisfied with the online format. The majority felt that they improved their knowledge of the subject area and were motivated to implement some of the strategies suggested. Suggestions

for further sessions included supporting the relatives, more strategies in how to integrate the knowledge in their roles and further online learning.

HPR 6

Improved Self-Management in Patients with Osteoporosis, Gout and Inflammatory Arthritis

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Background: The Swiss League against Rheumatism has developed a comprehensive self-management programme for patients with inflammatory arthritis (IA), gout and osteoporosis. In the course of this programme, sixteen medical assistants in outpatient rheumatological and general practitioner clinics were trained to strengthen the self-management capability of persons affected.

Objectives: The main objective of the programme is to increase the quality of life and level of health of patients with osteoporosis, gout and IA by enhancing their self-management capability. Furthermore, the project aims to support the professional development of medical assistants.

Methods: Using a questionnaire containing several validated measurement scales, data was collected at three points in time (t1 = enrollment of patient, t2 = last session of the self-management programme and t3 = two months after the last session). Descriptive statistical methods were used to analyse the data.

Results: In total 48 patients completed the programme until 2022. Overall, the results show a positive trend in self-management abilities and an improvement in the patients' current health status. Significant changes are seen in *Skill and Technique Acquisition* as well as in *Self-Monitoring and Insight* of the disease. Other components such as *knowledge* and *constructive attitudes and approaches* also underwent a small positive change. The *quality of life* has improved too and the *use of health services* indicates a slight decline after taking part in the self-management programme.

Conclusions: The comprehensive self-management programme designed by the Swiss League against Rheumatism proved to be successful. Knowledge about the disease, motivation to take action and skills to manage the disease improved significantly. The results also show a positive trend in the patients' current health status, their quality of live and a decline in disease activity. Further recommendations would be to strengthen the role of medical assistants even more, to establish structures which support self-management skills of patients suffering from chronic rheumatic conditions and to direct funds to self-management programmes.

Keywords: Self-Management capability, Health Care Professionals, Patient Information and Education, Rheumatic Diseases

HPR 7

Translation, Test-retest Reliability and Construct Validity of the German Version of the Exercise Self-Efficacy Scale in People with Axial Spondyloarthritis

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Background: Physical activity can improve disease-related symptoms in people with axSpA. In this context, self-efficacy for physical activity is an important predictive factor. The "Exercise Self-Efficacy Scale" (ESES) questionnaire can be used to assess self-efficacy for physical activity. However, a transculturally adapted German version of the questionnaire does currently not exist. Objective This study aimed to examine the transculturally adapted German version of the ESES (ESES-D) regarding its test-retest reliability, internal consistency, and construct validity in people with axSpA.

Method: The TRAPD Team Translation Model was used to translate the questionnaire in German. The ESES-D was subsequently evaluated in an observational study. The internal consistency was assessed using Cronbach's alpha and the test-retest reliability using the intraclass-coefficient (ICC, Two-way mixed effects model). Construct validity was examined based on a priori defined hypotheses using correlations between the ESES-D, demographic characteristics and measurement instruments on disease-related symptoms, functional limitations, physical activity, and outcome expectancy for training. The validity was considered valid if 6 out of 8 hypotheses were confirmed.

Results: The questionnaire was translated into German. 52 subjects between 31 and 80 years were included. The German version of the ESES indicated good values of reliability with an ICC of 0.78 (95 % CI; 0.63–0.88), and an alpha-coefficient of 0.85. 5 out of 8 a priori defined hypotheses were confirmed, thus, validity was not confirmed.

Conclusion: The ESES-D measures self-efficacy for physical activity with good test-retest reliability and internal consistency. Construct validity could not be terminatory confirmed. Further research on construct validity and responsiveness is recommended.

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EMH Swiss Medical Publishers Ltd.
Swiss Medical Weekly
Farnsburgerstrasse 8
CH-4132 Muttenz, Switzerland
office@smw.ch

ISSN online supplement: 2504-1622