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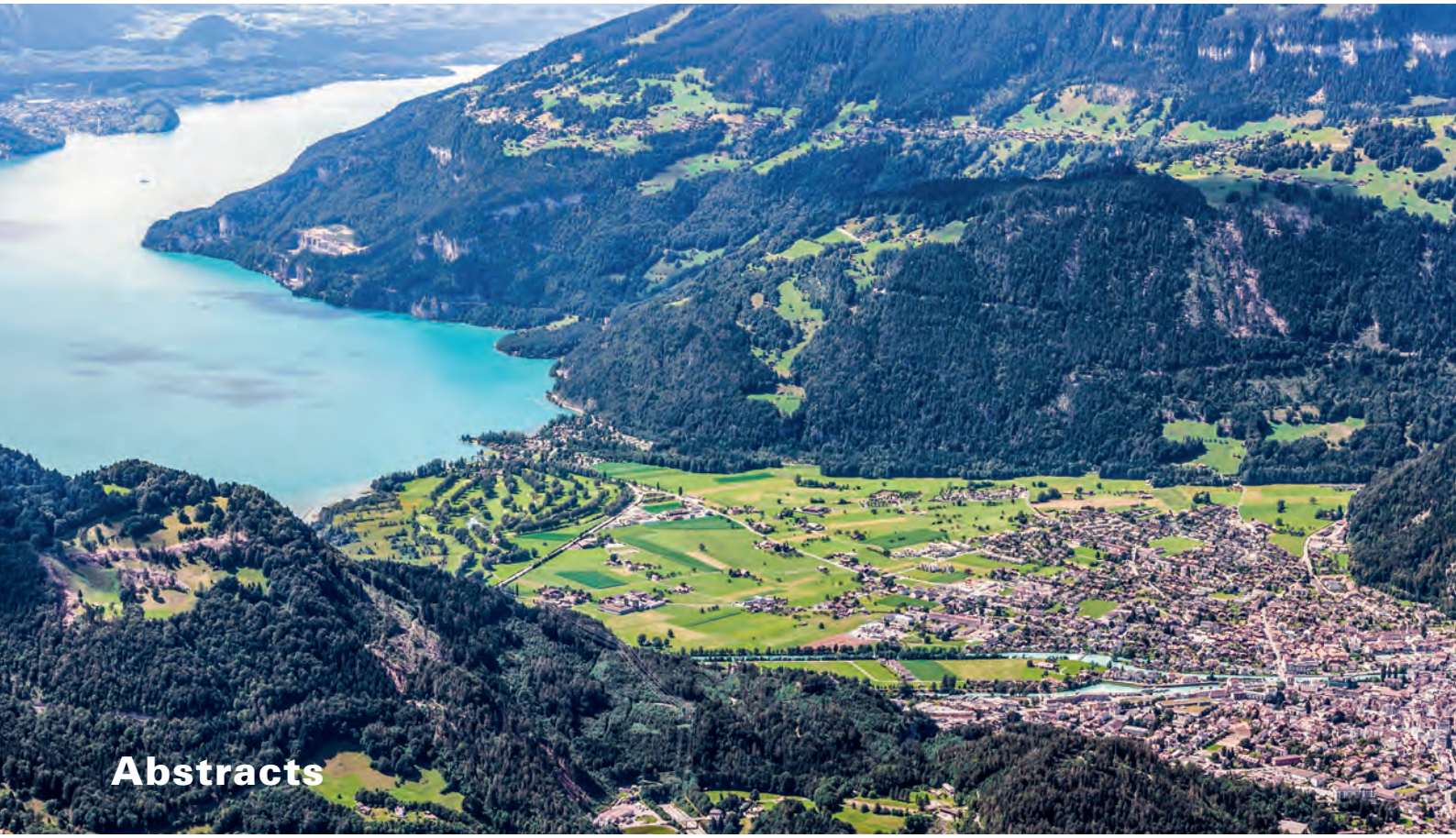

Abstracts

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BEST CASE SCENARIOS

Case 1

17q12 microdeletion syndrome as a cause of chondrocalcinosis

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Calcium pyrophosphate deposition (CPPD) diseases refer to rheumatic conditions due to calcium pyrophosphate crystals deposition. The term "chondrocalcinosis" is use mainly for the radiographic aspect of this disease. Being rare in patients younger than 60 years of age, that condition should lead to the research of an underlying metabolic favoring factor. We report a case of a woman of 43 years with severe chondrocalcinosis. A thoughtful evaluation allowed us to diagnose a familial 17q12 microdeletion syndrome and to broaden the clinical spectrum of this entity.

A woman of 43 years was seen in rheumatology for recurrent inflammatory joint complains. At time of referral, she had a tarsitis and an achilles tendinitis with sub-cutaneous tissue inflammation. Conventional radiography revealed severe chondrocalcinosis and tendon calcification at the feet, knees and wrists. She was known with maturity onset diabetes of the young (MODY), metabolic syndrome, stade 3 chronic kidney disease, a renal agenesis and a pancreatic head atrophy. Her familial history was also noteworthy with a son requiring an abdominal surgical procedure during the neonatal period and a left lobe hepatic atrophy.

The radiologic and clinical symptoms prompted us to consider a calcium pyrophosphate deposition disease. She was treated with anakinra (Kineret®) for 5 days with a complete response.

Her young age made us consider a metabolic condition promoting her joint disease and laboratory examination revealed a chronic hypomagnesemia due to renal wasting. Genetic testing demonstrated a heterozygous 17q12 microdeletion (including the Hepatocyte Nuclear Factor 1-beta (HNF1B) and LHX1 genes) in this family.

HNF1B encodes a member of the homeodomain-containing superfamily of transcription factors and mutations in this gene are the most commonly identified genetic cause of renal malformations. It seems also to regulate the renal epithelial ion transport via the Na+-K+-ATPase pump and 50% of patients with HNF1B mutations have hypomagnesemia. It explains the association of hypomagnesemia, type 5 MODY and the malformation syndrome.

A pubmed research with keywords including LHX1, HFN1B and 17q12 microdeletion did not reveal any rheumatic complains or CPPD disease in the reported cases, allowing us to broaden the clinical spectrum of this condition.

In conclusion, 17q12 microdeletion can promote CPPD disease secondary to hypomagnesemia. The rheumatic condition is incompletely reported in literature.

Case 2

A peculiar case of shoulder pain

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Background: Shoulder pain is a common symptom leading to physician consultation in primary care and rheumatology settings. The range of differential diagnoses is wide.

Case report: The formerly healthy 30-year old patient presented in our outpatient clinic with bilateral shoulder pain, which had started with no history of trauma two days earlier. Clinical findings were a painfull limited range of motion of the shoulders with a hematoma of the upper arm and a livid discoloration at the border of the tongue. Laboratory tests showed an increase of creatine kinase (4191 U/l, ULN 190 U/l), CRP (71mg/l, ULN 5 mg/l), ESR of 60mm/h and a slight microhematuria. ANA titer was 1:320 with negative ANCA as well as myositis- and anti-synthetase antibodies. A diagnostic puncture of the shoulder joint revealed hemarthrosis. Testing for HBV, HCV, HIV, EBV, CMV, Chlamydia, Gonococci and Lyme disease were unremarkable. A CT scan of the chest showed no abnormalities suspicious for infection or sarcoidosis. Suspecting a systemic vasculitis, a PET CT scan was performed. Surprisingly, it demonstrated fractures of the major tubercles of both humeri and a metabolically inactive lesion of the temporoparietal lobe. Subsequently, EEG was able to reveal focal epileptic potentials. In conclusion we diagnosed a first onset of secondary generalized epileptic seizure with consequent traumatic luxation and fracture of both shoulders, hemarthrosis, tongue bite with increased muscle and inflammatory markers. The temporoparietal lobe lesion was finally diagnosed as an astrocytoma WHO Grade III with cMRI and a neurosurgical resection was performed.

Discussion: In times of specialization and sub-specialization, it is of increasing importance to approach a medical symptom with a holistic view. On rare occasion, seldom, but potentially life-threatening diseases might hide behind presentations that could suggest trivial musculoskeletal disorders at first glance. These include well-known severe conditions like acute cardiac ischemia, aortic dissection, lung embolism or pneumothorax but can also encompass rarer causes like undiagnosed epilepsy. As an astute clinician it is therefore of utmost importance to always challenge one's primary and subsequent assessment when piecing together symptoms, clinical signs and findings.

Case 3

Dermatomyositis after treatment with antitumor immune checkpoint inhibitor: improvement with rituximab after TNF blocker failure

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Case report: A 65 years-old woman with metastatic non-small cells lung carcinoma was addressed to our department for evaluation of muscle weakness, myalgia and biological rhabdomyolysis, that appeared 2 weeks after the introduction of the anti-PD1 pembrolizumab. In the initial hypothesis of a non-specific, immunotherapy-related myositis, she had unsuccessfully been treated by her oncologists first with high doses of prednisone and then by an TNF-alpha-blocking agent. Complementary medical history revealed rapidly progressive proximal weakness of upper and lower extremities. She also presented typical skin findings (heliortope rash, Gottron's sign) and slight swallowing dysfunction. Immunological workup revealed high titers of antinuclear and anti-TIF1-gamma antibodies, confirming the diagnosis of dermatomyositis. Transient partial symptoms relief was achieved first with high dose (2g/kg) of intravenous immunoglobulins. In front of severe worsening with inability to walk and severe skin manifestations, she was further treated with 2 g rituximab, with significant improvement of skin and muscle function and the ability to walk again.

Discussion and conclusion: This case illustrates the great difficulties faced by clinicians with the occurrence, diagnosis and management of autoimmune paraneoplastic syndrome in the context of immune checkpoint inhibitor (ICI) treatments. Patients may be at particular risk given the conjunction of the risk conferred by the tumor itself, and the additional risk imparted by the ICI. In this case, the presence of anti-TIF1-gamma antibodies, well known to be associated with paraneoplastic forms of dermatomyositis, suggest that autoimmune processes were already evolving before ICI treatment. However, the fact that the disease manifested clinically soon after ICI introduction, together with the wide diversity of autoimmune manifestation that can be provoked by these treatments, indicates that the form that takes an auto-immune manifestation in this context depends on a sum of parameters associated to each patient, including genetics, comorbidities and treatments. Last, treatments such as IvIg and possibly B-cell directed therapies, that have the potential to spare the immune boost desired to fight the tumor are probably preferable to the sequence of high doses glucocorticoids eventually followed by TNF blockers that are frequently recommended indiscriminately in these situations.

Case 4

Vertebral tuberculosis in a patient treated with rituximab

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Introduction: Whe describe the case of a patient treated with rituximab (RTX) for a Sjögren syndrome

Case report: A 78-year-old woman with a Sjögren syndrome had been treated for 5 years with RTX i.v. perfusions (2g in 2013, followed the next year by 1g every 6 months). 18 months ago, she developed progressive low back pain in a context of degenerative changes with scoliosis and mild osteoporosis, and in May 2017 an osteoporotic fracture of the L1 superior endplate was diagnosed. The lumbar pain were again severe in autumn 2017, but stabilised with a brace, physiotherapy and antalgic medications (Ibuprofen, Paracetamol). However, 4 months later very severe back pain progressively recurred, especially during the night, with poor relief under opioid medications. An MRI showed abnormal modifications of L3 and L4 intervertebral space and vertebral bodies suggestive of Modic I changes. Given the severity of the symptoms, a biopsy L3 under CT scan control was performed and revealed mycobacterium tuberculosis by PCR. Cultures grew positive for mycobacterium tuberculosis. A retrospective investigation stated that she was screened for TB before (2013) and during rituximab therapy (2016), and experienced no risk of exposure to Tb, nor travels in regions hazardous for this disease; On the other hand she had worked in at risk developing countries before 2013. Of note, CRP and sedimentation rate always remained within the normal range. Expectorations were negative for tuberculosis.
She was treated with an anti-tuberculous quadritherapy (Rifampicin, Isoniazid, Pyrazinamid, Ethambutol) for 2 months, followed with Rifampicin and Isoniazid for 10 months. The lumbar pain decreased progressively and eventually completely resolved.
Discussion: The initial clinical presentation lead to investigate for supporting one of the following diagnosis: vertebral fracture, degenerative modification and non-Tb infection. The final diagnosis of vertebral tuberculosis came as a surprise and is to be considered between an acquired TB and an activated latent TB.
Conclusion: Rheumatologists should be aware that tuberculosis under immunosuppressive therapy can appear despite a negative screening for TB and the absence of fever and CRP elevation.

Case 5

A spontaneously resolving aortic stenosis

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The stenosis of the abdominal aorta and its branches is a pathological entity that can have different causes. The aorta is an elastic artery and a transient spasm at its level is unlikely. In contrast, Arterial spasms in the distal and muscular arteries such as the femoral, splenic and renal arteries have been described. We describe the case of a 56-year-old woman with spontaneously resolving aortic stenosis of the abdominal aorta.
A 56-year-old woman with cardiovascular risk factors with high blood pressure, diabetis and dyslipidemia. She has as antecedents, a multi-operated abdomen (inguinal hernia , ovarian cyst, abdominal flanges, hysterectomy). She complains of recurrent abdominal pain like cramps, not aggravated by the diet. An abdominal scan was performed, revealing the presence of a tight stenosis of the abdominal aorta measured at 5 mm at the height of the diaphragm and 5 mm in the anteroposterior axis upstream of the iliac bifurcation with parietal circumferential thickening of the aortic wall extending to the iliac and visceral arteries. The exhaustive clinical and paraclinical etiological assessment was negative. A PET scan was performed which unexpectedly revealed the disappearance of the narrowed aspect of the aorta and no sign of vasculitis. 6 months later, a control CT-Scan demonstrates a normal and regular caliber of the aorta.
This case illustrates an exceptional phenomenon of spontaneously resolving aortic stenosis evoking the hypothesis of aortic spasm. An extensive bibliographic search has found a single publication on a case of mesenteric ischemia on aortic spasm treated medically by vasodilators with a very good evolution. To our knowledge, this is the second case described in the literature.

PRESENTATION OF THE BEST ABSTRACTS

FC 1

Human lumbar spine facet joint osteoarthritis displays predominant NGF expression and signaling in synovial and subchondral bone marrow tissues

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Background: Treatment regimens for chronic low back pain (CLBP) are often not efficacious. Nerve growth factor (NGF) and its major receptor TrkA link tissue inflammation to pain. They regulate pro-inflammatory further downstream neurotransmitters such as substance P (SP). Inhibition of NGF has shown significant efficacy in osteoarthritis (OA) and in CLBP, but OA clinical trials have revealed rare cases of rapidly progressive OA (RPOA) of peripheral joints.
Objective: To describe the intensity and the tissue distribution of NGF, TrkA, SP and CD68+ macrophages in facet joint osteoarthritis (FJOA) of the lumbar spine.
Methods: FJOA specimens (n=10) were obtained by facetectomy from patients (average age 69 years, 5 males) undergoing intervertebral fusion. FJOA severity and synovitis was graded using preoperative MRI. Relative abundance of NGF, CD68 (macrophages), TrkA and SP in synovium (SY), cartilage (CL), subchondral bone (SB) and subchondral bone marrow (BM). Immunohistochemical tissue distribution was evaluated using a semi-quantitative scale ranging from 0-3. Association between imaging parameters and tissue expression was determined using Pearson correlation analysis.
Results: Synovitis was present in 6 cases and median Weishaupt grade of FJOA was 2 (1.5 – 3) corresponding with moderate to severe OA. Immunostain intensities (median [range]) were as follows: NGF: SY (3 [0-3]) and BM (1 [0-3]). TrkA: SY (0 [0-1]) and BM (3 [2-3]). CD68: SY (0.5 [0-1]) and BM (3 [2-3]). SP: SY (3 [1-3]), CL (2 [1-3]) and BM (3 [2-3]). NGF in SY and BM were strongly correlated (r=0.94), but not to synovitis or FJOA severity. The relative abundance of macrophages and NGF was strongly correlated exclusively in SY (r = 0.78).
Conclusion: NGF expression and signalling is present in FJOA, but not strongly associated with synovitis or osteoarthritis severity. These results are in agreement with recent studies of human knee OA, which have shown osteochondral NGF expression as a hallmark of symptomatic OA independently of chondropathy or synovitis. Targeting NGF in CLBP and FJOA might affect pathomechanisms in SY and BM tissues.

FC 2

The predictive value of rheumatoid factor, anti-citrullinated protein antibodies, anti-carbamylated protein antibodies and anti-peptidyl arginine deiminase type-3 antibodies, alone or in combination, on radiographic damage in rheumatoid arthritis

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Background: Autoantibodies such as anti-citrullinated protein antibodies (ACPA), anti-carbamylated protein antibodies (CarP) and anti-peptidyl arginine deiminase 4 (PAD4) antibodies have been associated with disease severity and radiographic progression in rheumatoid arthritis (RA). However, very little is known about the anti-PAD 3 (PAD3) antibodies and of the added value of combining multiple autoantibodies to predict radiographic damage.
Objectives: To investigate the capability of rheumatoid factor (RF), ACPA, anti-CarP and anti-PAD3 antibodies to predict radiographic damage in RA.
Methods: We performed a nested cohort study within the « Swiss Clinical Quality Management » (SCQM) RA registry. Biobank samples were tested for RF, ACPA (anti-CCP3), anti-CarP and anti-PAD3. Outcome: radiographic damage assessed with the Ratingen score. We examined the association of each autoantibody both separately and combined, with radiographic damage at baseline and over time with linear mixed-effects models.
Results: A total of 851 RA patients were included with a median of 4 Ratingen scores per patient. Autoantibodies were positive in the following proportion of patients: RF IgM 66.3%, RF IgA 56.9%, ACPA 63.8%, anti-PAD3 10.7% and anti-CarP 22.4%. Significantly higher baseline Ratingen scores were associated with the presence of RF (IgM and IgA) and ACPA and greater progression over time with RF IgM and ACPA (p=0.01 and p=0.04 respectively). Patients' positive for anti-PAD3 demonstrated significantly higher mean baseline Ratingen scores compared with anti-PAD3 negative patients (14.9 vs. 8.8 respectively). In the ACPA negative subgroup (n= 308), baseline Ratingen scores were significantly higher in anti-PAD3 positive patients (p=0.01).There were no significant differences with regards to anti-CarP. The presence of at least 3 of the following autoantibodies: RF IgM, ACPA, anti-CarP and anti-PAD3, was associated with significantly greater radiographic progression over 10 years than if these autoantibodies were absent (p=0.03).
Conclusions: The presence of anti-PAD3 antibodies was associated with significantly higher scores of radiographic damage at baseline, in both the overall population and in the subgroup of ACPA-negative patients. Combinations of autoantibodies (including anti-CarP and anti-PAD3) predicted both higher baseline radiographic damage and greater radiographic progression over time.

FC 3

Disturbed PD-L1 upregulation is characteristic of B cells in SLE

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Background: Prior studies on systemic lupus erythematosus (SLE) B cells reported an altered responsiveness to TLR9 stimulation, such as proliferation, cytokine production as well as indications for impaired T and B cell interaction [1]. The role of co-inhibitory and co-stimulatory (check-point) molecules in this setting has not been delineated in detail so far.
Objective: Assess the expression of co-inhibitory (PD-1, PD-L1 and PD-L2) and co-stimulatory molecules (CD86 and CD40) by SLE B cells after in vitro stimulation and their potential contribution for B cell hyporesponsiveness in SLE.
Methods: PBMCs from 10 SLE patients and 10 healthy donors (HD) were stimulated with IL-2/IL-10, anti (α) - B cell receptor (BCR), CpG and CD40L alone or in combination. Expression of PD-1, PD-L1, PD-L2 as well as CD86, CD40 on CD19+CD20+ B cell subsets after 48h stimulation was analyzed by FACS. CD71 was employed to measure proliferation of CD19+CD20+ B cells after 48h stimulation.
Results: SLE B cells exhibited a substantially decreased upregulation of PD-L1 (p = 0,0006) and CD 86 (p = 0,0188, Fig.1) associated with significantly reduced B cell proliferation (p = 0,0039) after 48h stimulation with CpG alone and in combination compared with HD. While TLR9 engagement in SLE B cells appeared to be abnormal, activation of CD40 resulted into a consistent upregulation of both, inhibitory and stimulatory molecules. PD-L1 was positively correlated with B cell proliferation (p = 0.003). Notably, the expression of PD-L1 and CD 86 correlated inversely with Siglec-1, as surrogate marker for Type I interferon signature (IFN-I, p <0,0001 and p = 0.0021 respectively). PD-L1 expression correlated inversely with cSLEDAI (p = 0.0087).
Conclusions: Hyporesponsive lupus B cells are characterized by a functionally diminished PD-L1 and CD86 upregulation associated with IFN-I signature. Reduced upregulation capacity of PD-L1 correlated also with clinical activity and reduced proliferation. The data mandate evaluations of innovative therapeutic interventions in SLE.

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POSTERS

P 1

The impact of pregnancy on structural progression in premenopausal women with rheumatoid arthritis

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Background: Disease activity often improves during pregnancy and worsens at the postpartum period. The long-term effect of pregnancy on radiographic joint damage progression among premenopausal women with RA has been barely studied.
Objectives: The aim of this study was to analyse the impact of pregnancy on radiographic progression in premenopausal women with RA.
Methods: This is an observational cohort study of RA patients included in the SCQM-RA. Patients enrolled are followed-up and have radiographic assessments at regular intervals. Information about female reproductive factors, such as pregnancies, breastfeeding and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included premenopausal women with at least two radiographic assessment and full information on reproductive factors. The primary outcome was the rate of radiographic progression. We analysed the radiographic progression between premenopausal women with at least one pregnancy and those with no pregnancies. Baseline time was the first radiographic assessment. We used a multilevel regression model for longitudinal data, adjusted for potential confounders, such as baseline age, disease duration, DAS-28 and treatment.
Results: A total of 430 premenopausal women were analysed, half of which had at least one pregnancy. Women with at least one pregnancy were older than nulliparous (median of 41 vs 36 years, $p<0.001$) and had longer disease duration (median of 3.4 vs 2.6 years, $p = 0.04$). During follow-up, the rate of radiographic progression was lower in women with pregnancies than in nulliparous women [(0.9% (95% CI: 0.0 to 1.9) vs 2.1% (95% CI: 0.9 to 3.1) over 10 years, respectively, $p = 0.04$]. In a sub-analysis, the rate of radiographic progression appeared to be lower during the 13-year period after first pregnancy than after this period [(0.2% (95% CI: -0.8 to 1.3) vs 2.6% (95% CI: 1.3 to 3.9) over 13 years, respectively, $p = 0.003$]. We found no difference in the rate of radiographic progression between women with a single pregnancy and multiparous women.
Conclusion: In premenopausal women with RA, joint damage progressed more rapidly in nulliparous women than in women with at least one pregnancy. However, we cannot make any definite causal inference, since it is well possible that women renouncing getting pregnant might be patients with more severe disease. Radiographic progression appeared to increase the longer the time since pregnancy.

P 2

Rheumatoid arthritis, biological treatment and Echinococcus multilocularis infection

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Introduction: Immunosuppression linked to inflammatory arthritis and their treatments favours the risk of viral and bacterial infection. The increased risk of parasitic infection is still controversial. The case presented here describes the occurrence of an Echinococcus multilocularis infection in a rheumatoid arthritis (RA) patient treated with a biological agent.
Case: A woman born in 1951 has been suffering from seropositive RA since 2014. In 2014, she reported episodes of haemoptysis. A CT-scan showed several pulmonary nodules, which grew during the two following years, as shown by a check CT-scan in 2016. Investigations (bronchoscopy, transthoracic puncture) concluded to rheumatoid nodules. Tocilizumab was then changed for abatacept. In March 2018, a new thoracic CT revealed a mass in the anterior wall of the right ventricle. A myocardic biopsy showed normal fragments of myocardium and excluded a tumour or an inflammation process.
In May 2018, the patient consulted an emergency unit because of left hemi-ataxy, headache and dizziness. A cerebral MRI revealed multiple cystic lesions suggesting an infectious origin. Blood serology and PCR of a pulmonary nodule were positive for Echinoccocus multilocularis. The diagnosis of multisystemic alveolar echinococcosis was retained. A life-long treatment of albendazole was begun. To date evolution is good.
Discussion: Echinococcus multilocularis infection associated with inflammatory arthritis and their treatments are extremely unusual (1-2). In Switzerland, the incidence of echinococcosis in autoimmune arthritis appears to be higher than in general population but remains very low (3). A few case reports (4) and some experimental animal studies (5) have suggested that parasitic infections could be favoured by immunosuppression due to inflammatory arthritis and their treatments.
Conclusion: Autoimmune arthritis and their treatments may favour the occurrence of parasitic infection but large-scale studies are needed to confirm this hypothesis.

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P 3

Concurrent calcium pyrophosphate deposition arthritis and rheumatoid arthritis succesfully treated by tocilizumab.

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Background: Calcium pyrophosphate deposition (CPPD) arthritis and rheumatoid arthritis (RA) can be potential mimickers and concurrent diseases. Indeed, recent studies suggest a positive association between the two diseases, with a prevalence of CPP crystals in RA patients up to 25%. Although an etiological connection between CPPD and RA is still lacking, CPPD is thought to be a late complication of longstanding RA. Neverthless, simultaneous diagnosis of both CPPD and RA is possible.
CPP crystals induce inflammatory response involving IL-6 mainly through the NALP3 inflammasome and IL-1 pathway. Anti-IL-1 medication is therefore used effectively in some cases of CPPD arthritis resistant to classical medications. Tocilizumab, an anti-IL-6 used for the treatment of moderate to severe and resistant RA, has recently shown exciting results in the management of two cases of CPPD arthritis resistant to anti-IL-1.
Here, we report a case of a 66-years-old man with concurrent CPPD arthritis and seropositive RA successfully treated by tocilizumab.
Case presentation: The patient suffered from chronic peripheral polyarthralgia and polyarthritis on a rather asymetrical and migratory pattern, affecting predominantly the medium-large joints but also the small ones in a lesser extend. Laboratory findings demonstrated an inflammatory syndrome, rheumatoid factor and anti-cyclic citrullinated peptide positivity. No RA typical lesion, but chondrocalcinosis (CC) of the right knee, pubic symphisis and left hip was seen on plain radiographs. Ultrasound confirmed the CC in knee and hip and CPP crystals were isolated in inflammatory synovial fluid samples from these two joints. Pulmonary exams demonstrated an intersitial pneumopathy. The diagnosis of seropositive RA and CPPD arthritis were retained, according to the ACR/EULAR classification criteria and recommandations.
The diseases were still clinically and biologically active despite the successive use of NSAIDs, glucocorticoids, leflunomide and colchicine. Tocilizumab (8mg/kg IV) was started at this point, with major improvements of symptoms and clinical status, and normalization of the inflammatory markers.
Conclusion: In CPPD arthritis pathomechanisms, IL-6 is one of the major pro-inflammatory cytokine involved, mainly stimulated via the NALP3 inflammasome/IL-1 pathway. IL-6 blockade, currently used in RA, could be an interesting treatment option next to anti-IL-1 and classical treatments for CPPD, especially in patients with concurrent RA.

P 4

Tocilizumab in a patient with rheumatoid arthritis secondary to checkpoint inhibitor therapy - a case report

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Background: The emerging use of immune checkpoint inhibitors in oncology for a variety of malignancies has led to an increase of immune related adverse events (irAE). IrAE often require interdisciplinary consideration and management. We present a case of steroid refractory rheumatoid arthritis (RA) secondary to immune checkpoint inhibitor therapy in malignant melanoma, successfully treated with an IL-6-receptor inhibitor, tocilizumab, and achieving remission according to the Disease Activity Index (DAS) 28.
Case presentation: A 57-year-old female patient with a history of non-pigmented melanoma was treated with pembrolizumab, a programmed death receptor ligand 1 (PD-L1) antibody (200 mg/Q3W, intravenous) from November 2017 to July 2018. 4 months after the first administration of pembrolizumab, she developed morning stiffness and polyarthritis with joint swelling (mainly knee and finger joints). The patient was evaluated in our rheumatology department, which revealed active polyarthritis (with swelling of the elbows, wrists, the right knee and all small joints of both hands) and morning stiffness. Ultrasound of the right knee showed bursitis of the suprapatellar recessus and positive Doppler signal in the lateral aspect of the knee. Magnetic resonance imaging studies confirmed synovitis of the right knee. We established the diagnosis of RA secondary to immune checkpoint inhibitor therapy. The patient was treated with prednisone orally (initial dose 100 mg/d in a tapering scheme) with moderate response to steroid dosage below 30 mg. Tocilizumab (8 mg/kg body weight, administered every 4 weeks, intravenous) was started 2 months later. After 3 cycles (12 weeks) of tocilizumab, symptoms improved significantly and prednisone was successfully tapered and stopped after 5 months. DAS 28 score improved from 6.28 to 2.08 after 5 months of therapy with tocilizumab. No tumor progression was noted (clinically and by imaging). We continued tocilizumab as a remission maintenance therapy for RA.
Conclusion: Tocilizumab may be a safe and efficient treatment option in steroid refractory arthritis secondary to checkpoint inhibitor therapy. Further randomised studies are needed to evaluate safety, efficiency and long-term effects of tocilizumab in rheumatoid arthritis secondary to PD-L1 inhibition.

P 5

Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response or Intolerance to Biological DMARDs: Results at 60 weeks from the SELECT-BEYOND Study

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Background: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response or intolerance to bDMARDs, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, resulted in significant improvements over 24 weeks (wks).1
Purpose: We assessed UPA safety & efficacy through Wk60 in an ongoing extension of the phase 3 SELECT-BEYOND study.
Methods: A population of pts with active RA who had failed at least one prior biologic therapy was enrolled.1 Pts received UPA 15mg or 30mg once daily (QD) or placebo (PBO) on csDMARD background for 12 wks. From Wk12, pts randomized to UPA at baseline (BL) continued their assigned doses, while pts initially randomized to PBO received UPA 15mg or 30mg QD per pre-specified assignment at BL. Pts who completed Wk24 entered the blinded long-term extension. Adverse events (AE) per 100 pt years (PY) are summarized based on a cut-off date of 16 April 2018. Efficacy data up to the Wk60 visit are reported "As Observed".
Results: 418/498 pts were randomized, completed 24wks & entered the extension on study drug. By the safety data cut-off date, 19% pts discontinued study drug: 5/4/3/2/5% due to AE/lack of efficacy/withdrew consent/lost to follow-up/other reasons. Cumulative exposures to UPA15 and UPA30 were 301.7 and 290.7 PYs, respectively. Rates (Events/100PYs) of treatment-emergent AEs were numerically higher in the UPA30 vs UPA15 arm for serious AEs, AEs leading to discontinuation, serious infections, herpes zoster & hepatic disorders. Based on As Observed analysis, for pts completing Wk60 on UPA15 [172/216 (80%)] and UPA30 [168/202 (83%)], clinical & functional outcomes continued to improve compared to BL, or were maintained from Wk24 onwards1 in pts initially randomized to UPA15 or 30; Remission by CDAI≤2.8 at Wk60 was achieved by 20% and 32%, respectively, and DAS28-CRP<2.6 was achieved by 53% and 52%. Pts who were switched to UPA from PBO at Wk12 had comparable efficacy to pts initially randomized to UPA.
Conclusion: The benefit:risk of UPA treatment in this refractory population remains favorable. No new safety signals were identified. Some AEs were numerically higher for UPA30 vs 15; however its clinical significance, assessment of rare safety events, and overall benefit:risk of UPA15 & 30 in RA treatment are best evaluated in an integrated analysis. UPA15 & 30 continued to be effective in treating RA signs & symptoms, and in improving physical function.

Reference:
1 Genovese et al 2018; Lancet.18;31116-4

P 6

Summary of indirect comparisons to evaluate efficacy of baricitinib with targeted synthetic and biologic disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis

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Objective: We summarize findings from matching-adjusted indirect comparison (MAIC) and network meta-analysis (NMA), conducted in conventional synthetic/biologic disease-modifying anti-rheumatic drug (cs/b DMARD)-naive and methotrexate inadequate responder (MTX-IR) populations, respectively.
Methods: Systematic literature reviews were performed for MAIC and NMA. For MAIC, pain (visual analog scale [VAS], 0-100 mm) and HAQ-DI were evaluated. Individual patient (pt) data from RA-BEGIN baricitinib (BARI) 4mg arm were weighted to match baseline characteristics of PREMIER adalimumab (ADA) 40mg arm, ORAL-START tofacitinib (TOFA) 5mg arm and tocilizumab (TCZ) 8mg/kg arm from AMBITION+FUNCTION, respectively; MTX arms were also matched between trials. After adjustment, mean changes in pain VAS and HAQ-DI at Week (Wk) 24 for BARI were indirectly compared with published results for Wk 24 TCZ and TOFA and Wk 26 ADA data. NMAs of randomized controlled trials reporting American College of Rheumatology (ACR) response data (24 trials) were conducted on approved drug dosages using Bayesian mixed-treatment comparisons.
Results: Across MAIC trials, in MTX arm, mean baseline pain VAS was 58.7-65.2 (6-month mean change in pain: −28.3-33.5), indicating comparability between trials. Similar HAQ-DI and changes in HAQ-DI were observed. At Wk 24, statistically significant pain improvements were observed for BARI vs ADA ($p \leq 0.001$) and TCZ ($p \leq 0.05$). For TOFA, these improvements were only observed with Bucher method ($p \leq 0.05$). Improvement in HAQ-DI was significantly greater in BARI than TCZ ($p \leq 0.05$) and ADA ($p \leq 0.001$), but not TOFA. NMAs using RA-BEAM data showed BARI 4mg to be more effective than ADA (odds ratio [OR] 1.33; 95%-credible interval [CrI] 1.01-1.75), abatacept (ABA) (OR 1.47; 95%-CrI 1.02-2.13), infliximab (OR 1.61; 95%-CrI 1.12-2.27) for ACR20. While no differences were found on ACR50, BARI 4mg was found to be more effective than ADA and ABA for ACR70.
Conclusions: In cs/b DMARD-naive pts with RA, results from MAIC showed statistically significant pain reduction and improved physical function for BARI monotherapy vs TCZ and ADA monotherapy. Results from NMA support advantage of BARI as a treatment option for patients with moderate-to-severe RA with inadequate response to MTX.

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P 7

Association between baseline hemoglobin levels and radiographic joint damage progression in patients with rheumatoid arthritis treated with baricitinib or standard of care

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Objectives: To assess the association between baseline Hb levels and structural damage progression and study the effect of BARI 4-mg once daily on structural damage progression at 52 weeks (wks) based on baseline Hb levels.
Methods: Data from the modified intention-to-treat populations of RA-BEGIN (MTX = 210/BARI 4-mg = 159/BARI 4-mg+MTX = 215 patients) and RA-BEAM (placebo [PBO] = 488/adalimumab [ADA] = 328/BARI 4-mg = 487 patients) were analyzed. Structural damage progression is the change from baseline (CFB) greater than the smallest detectable change (SDC) in modified total Sharp score (mTSS) at wk52; RA-BEGIN SDC: 1.4; RA-BEAM SDC: 1.5. Missing mTSS data at wk52 were imputed using linear extrapolation based on baseline data and most recent radiographic data prior to missed radiograph. The number of patients with CFB in mTSS>SDC at wk52 were calculated for low (males/females: <13/<12g/dL) or normal baseline Hb for each treatment arm from both studies. Multivariate logistic regression (MLR) was used to study the association of baseline Hb with structural joint damage at 52 wks. MLR included treatment; baseline values of Hb, hsCRP, CDAI, HAQ-DI, and joint erosion status; BMI; smoking status; and geographical area. Patients with missing baseline/post-baseline radiographic data (RA-BEGIN: 39/RA-BEAM: 68) were excluded from MLR analyses; as were patients with missing data for covariates of MLR (RA-BEGIN: 7/RA-BEAM: 19). All analyses were post-hoc.
Results: Overall, patients with higher baseline Hb were less likely to show CFB in mTSS>SDC (RA-BEGIN: adjusted odds ratio [OR] = 0.72, p = 0.001; RA-BEAM: adjusted OR = 0.76, p<0.001) at 52 wks, independent of other factors of the MLR model. In RA-BEGIN, CFB in mTSS>SDC was less frequent in patients with low baseline Hb receiving BARI alone or BARI+MTX vs those on MTX alone; in patients with normal baseline Hb, difference between treatments was less pronounced. In RA-BEAM, CFB in mTSS>SDC was less frequent in patients with low or normal baseline Hb receiving BARI or ADA vs PBO.
Conclusions: In RA patients, lower baseline Hb levels were associated with increased structural damage progression. Treatment with BARI 4-mg reduced structural progression irrespective of baseline Hb status; structural progression at 52 wks was more pronounced in patients with low baseline Hb receiving MTX alone (RA-BEGIN) or PBO and background MTX (RA-BEAM).

P 8

A comparative analysis of upadacitinib monotherapy and upadacitinib combination therapy for the treatment of rheumatoid arthritis from two

Phase 3 trials

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy & safety in patients (pts) with rheumatoid arthritis (RA) as monotherapy (mono) and in combination (combo) with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX).1,2 However, UPA mono has not been compared directly with UPA combo in the Phase 3 program.
Objectives: To compare the efficacy of UPA mono & UPA combo with MTX using data from two Phase 3 trials of RA pts with an inadequate response (IR) to prior MTX therapy.
Methods: In SELECT-MONOTHERAPY, 648 MTX-IR pts were randomized to receive UPA 15mg or 30mg mono once daily (QD), or continue with MTX mono (cMTX; blinded study drug), for 14 weeks. In SELECT-NEXT, 661 csDMARD-IR pts were randomized to receive UPA 15mg or 30mg QD or placebo (PBO) for 12 weeks on csDMARD background. Primary endpoints were the proportion of pts achieving ACR20 & DAS28(CRP) ≤3.2. Additional endpoints included ACR50/70, DAS28(CRP) <2.6, CDAI remission (≤2.8), CDAI low disease activity (LDA; ≤10), and change from baseline in HAQ-DI. Logistic regression or ordinary least squares analyses were used to compare outcomes with mono vs combo, adjusting for demographics & baseline disease characteristics.
Results: A total of 1114 pts were included, of whom 648 received mono in SELECT-MONOTHERAPY & 466 received combo in SELECT-NEXT. Of the pts receiving combo, 338 (72.5%) were receiving MTX background therapy only and 128 (27.5%) were receiving MTX + other csDMARDs. Baseline characteristics were similar between study cohorts; the majority of pts were female and of white ethnicity, with a mean age of approx. 55years & a mean MTX dose of approx. 17mg/week. Both UPA mono & UPA combo led to significant improvements in efficacy outcomes versus cMTX/PBO+MTX. No significant differences were observed between UPA mono & UPA combo across a range of clinical endpoints, including ACR20/50/70 responses & measures of LDA & remission. Improvements in quality of life were similar with UPA mono & combo. Efficacy was comparable between the two UPA doses in the combo group, whereas in the mono group numerically higher responses were observed with UPA 30mg vs UPA 15mg.
Conclusions: In MTX-IR pts with RA, the efficacy of UPA appears comparable when administered as mono or when given in combo with MTX.

References

1 Smolen J, et al. Ann Rheum Dis 2018;77:67-8
2 Burmester GR, et al. Lancet 2018;391:2503–12

P 9

A comparison of upadacitinib plus methotrexate and upadacitinib plus other csDMARDs in patients with rheumatoid arthritis: An analysis of two phase 3 studies

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has shown efficacy in patients (pts) with rheumatoid arthritis (RA) when combined with methotrexate (MTX) or other conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).1,2 However, the efficacy of UPA plus MTX has not been directly compared with UPA plus other csDMARDs.
Objectives: To compare the efficacy of UPA in combination with MTX versus UPA in combination with other csDMARDs in pts with an inadequate response (IR) to csDMARDs (SELECT-NEXT1) or biologic DMARDs (bDMARDs; SELECT-BEYOND2).
Methods: 661 pts in SELECT-NEXT and 498 pts in SELECT-BEYOND received UPA15mg or 30mg once daily (QD) or placebo (PBO) for 12 weeks; all pts received concomitant csDMARD(s). The primary endpoints for both studies were rates of ACR20 response and DAS28(CRP) ≤3.2. Additional endpoints included DAS28(CRP) <2.6, CDAI low disease activity (≤10), and CDAI remission (≤2.8). Pts were grouped according to concomitant csDMARD use (MTX vs non-MTX csDMARDs); pts receiving both MTX and a non-MTX csDMARD were included in the MTX group.

Results: In SELECT-NEXT and SELECT-BEYOND, 535 and 410 pts, respectively (~80%), were receiving concomitant MTX (mean dose 17mg/week), and 124 and 82 pts were receiving non-MTX csDMARDs. Demographics and disease characteristics were broadly similar between treatment groups; the majority of pts were female and of white ethnicity, and around half were using oral corticosteroids at baseline. Across all subgroups, the proportion of pts achieving efficacy outcomes was higher with both UPA doses compared with PBO. There were no significant differences between efficacy outcomes with UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs in either pt population. This included ACR20 response as well as low disease activity and remission defined by DAS28(CRP) and CDAI.
Conclusions: In this post hoc analysis, the efficacy of UPA in pts with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.

Reference

1 Burmester GR, et al. Lancet 2018;391:2503–12; 2. Genovese MC, et al. Lancet 2018;391:2513–24

P 10

Safety of baricitinib: update from up to 6 years of treatment in rheumatoid arthritis clinical trials

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Background/purpose: Baricitinib (BARI), an oral, selective inhibitor of Janus kinase (JAK1 and JAK2), is approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults in over 50 countries. This abstract provides an update on the safety profile of BARI up to 6 years of treatment in RA clinical trials.
Methods: Data were pooled from 8 randomised trials (4 Phase 3, 3 Phase 2, 1 Phase 1b) and 1 long-term extension (LTE) study (data up to 01-April-2017). The safety data were analysed in 3 integrated datasets: placebo (PBO)-controlled (6 studies comparing BARI 4-mg QD to PBO 0-24 weeks), extended BARI (4 studies with BARI 2- and 4-mg QD, including LTE data) and ALL-BARI-RA (all patients exposed to ≥1 dose of BARI from 8 randomised trials and LTE). Incidence rates (IRs, per 100 patient-years [PY]) for safety events with 95% CIs are reported.
Results: In total, 3492 patients were exposed to BARI for up to 6 years (7860 PY of total exposure; median: 2.5 years). The IRs for serious infections, malignancies, major adverse cardiovascular events, arterial thrombotic events, and venous thromboembolism did not increase with prolonged exposure. During the 24-week PBO-controlled period, deep vein thrombosis (DVT)/pulmonary embolism (PE) was reported with BARI 4-mg (n = 6/N = 997) but not with PBO. However, this was not observed during the first 24 weeks after switch to BARI 4-mg from PBO (n = 1/N = 928) or active comparator (adalimumab/methotrexate; n = 0/N = 451). At longer exposures, DVT/PE IRs were comparable between BARI 2- and 4-mg doses and the overall IR was 0.53. The IRs for gastrointestinal perforation and tuberculosis were 0.04 and 0.14, respectively in All-BARI-RA dataset.
Conclusion: The safety profile of BARI up to 6 years of treatment in RA clinical trials remained consistent with the profile previously reported and remains acceptable in the context of demonstrated efficacy.

P 11

Reduction of vertebral fractures and rapid loss of bone after discontinuation of Denosumab: A cohort study of 97 postmenopausal women treated with denosumab for 2 years, followed by a single infusion of zoledronate

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Background: Discontinuation of denosumab is associated with rapid loss of bone mineral density (BMD) back to baseline and may be associated with an increased risk of vertebral fractures. No sequential treatment has been established yet on how to prevent either the loss of BMD or to prevent rebound fractures after discontinuation of denosumab. The aim of this 8-year cohort study in a resident rheumatology practice was to investigate the effect of a single zoledronate infusion, administered 6 months after the last denosumab injection on the occurrence of fractures and on rapid loss of BMD.
Methods: 97 women with postmenopausal osteoporosis were treated with denosumab 60 mg every 6 months for 2 years and one single infusion of 5 mg zoledronate 6 months after the last denosumab injection. Patients were controlled clinically, by DXA and by vertebral fracture assessment before the first denosumab injection, after 2 years and after 4 years. Subgroup analyses were made for patients with or without prevalent fractures, prior bisphosphonate treatment and lumbar spine BMD gain of >9% versus <9%.
Results: 1½ - 2½ years after the last denosumab injection 2 vertebral fractures (1.1% per 100 patient years), and 3 non-vertebral fractures (1.7% per 100 patient years) had occurred. Multiple vertebral fractures were not observed. 64% (CI: 52-81%) of BMD gain was retained at lumbar spine, 52% (CI: 26-72%) at total hip. There was no significant difference in decrease of BMD in patients with BMD gain of >9% vs. <9% while treated with denosumab. Previous antiresorptive treatment or prevalent fractures had no impact on decrease of BMD. Patients controlled 1.5 versus 2.5 years after the last denosumab injection had comparable decrease of lumbar spine BMD, suggesting that the entire loss of BMD occurs between 6-18 months after the last denosumab injection.
Conclusions: A single infusion of zoledronate reduces the risk of rebound vertebral fractures after discontinuation of denosumab patients treated for postmenopausal osteoporosis. Some patients, especially those with a high risk for osteoporotic fractures, may need to be treated with bisphosphonates longer than one year.

P 12

Can we avoid the loss of bone mineral density one year after denosumab discontinuation? The ReoLaus Bone Project

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Objectives: Denosumab discontinuation (DD) induces bone turnover markers (BTMs) increase, bone mineral density (BMD) decrease, and increased risk of spontaneous vertebral fractures. Prescribing a bisphosphonate after DD could avoid this rebound effect. The objective of the ReoLaus (Rebound Effect Observatory in Lausanne) Bone Project is to follow bone parameters after DD. We report the determinants associated to BMD loss 1 year after DD.
Methods: 170 patients are followed in ReoLaus. Patients with a BMD follow-up >1 year after DD with a standardized management were included. We defined as significant a lumbar spine BMD loss (Loosers group) over 3.96% at one year after DD as compared with values at the end of the denosumab treatment 18 months after last injection.
Results: 71 post-menopausal women stopped denosumab after 7.7±2.2 injections: age 63.8±8.1 years, BMI 23.8±4.5, 0.96 prevalent fractures/patient, 8.45% previously exposed to corticoids, 22.54% to anti-aromatases. 17.25 months after last denosumab injection 30 patients were classified as Loosers and 41 as Stable. At denosumab introduction Loosers were younger (61.4±7.3 vs 65.5±8.2 years, p = 0.034) with higher sCTX level (644.7 vs. 474.1 ng/ml, p = 0.005). The rate of BP given less than 2 years before denosumab was not different, but none of the Loosers had received zoledronate vs. 12% of the Stable (p = 0.047). Other pre-denosumab characteristics were not different. Number of denosumab injections, BTMs and BMD values were comparable in both groups during denosumab treatment. First BTMs values measured 7.5 months (median) after last denosumab injection and before bisphosphonates were not different (sCTX: Loosers, 592 ng/ml; Stable, 379 ng/ml, p = 0.06). At DD 59% received zoledronate, 24% alendronate, 3% others, and 14% nothing (p = 0.39 between groups). BTMs 12.8 months post-BP were higher in Loosers as compared to Stable (sCTX 537 vs. 336 ng/ml, p = 0.009). Incidence of new fractures was low (0.18/patient) without between group's difference.
Conclusion: In our sub-cohort, being younger, having high BTMs and not having received zoledronate before denosumab introduction increases the risk of a BMD loss, even if a bisphosphonate is prescribed at DD. Our results support the use of denosumab after a bisphosphonate to restrain the BMD loss at its discontinuation and a strategy to maintain BTMs as lowest as possible after DD.

P 13

Bone health in patients with psoriasis arthritis in a Swiss cohort

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Introduction: The effect of psoriatic arthritis (PsA) on bone mineral density (BMD) is not well understood and there is much controversy regarding loss of bone mass in patients with PsA. We analyzed data from the Swiss Clinical Quality Management (SCQM) cohort, which is a large national cohort database of patients with inflammatory arthritis.
Patients and methods: We analyzed 2443 consecutive patients included in the cohort between September 1997 and April 2019. We evaluated demographic and clinical characteristics assessed in the SCQM cohort, such as age, gender, body mass index (BMI), disease duration, smoking and alcohol habits, patient's and physician's global assessment, American College of Rheumatology (ACR) joint count, inflammatory activity measured by erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), disease activity score (DAS 28), quality of life assessed by health assessment questionnaire (HAQ), rheumatoid factor, anti-CCP, HLA B27 status and medication use. First, we compared the patient group with bone density measurement (DXA) with the group with no DXA. In a subgroup analysis we compared DXA patients according to their osteoporotic status..
Results: Patients with DXA were on average 6 years older (54.27±11,12 vs 47.8±12,48 years, p<0.001), and were more likely to be female (67.8% vs 43.4%) than the patients without DXA. The duration of the disease was longer (6.67±8,35 vs 5,30±7,12 years, p<0,001) in the DXA group. CRP and ESR were also higher in the DXA group (10,27±20.61 vs 8.21±10.94 mg/L, p<0,001 and 17,10±17,63 vs 15,13±15,21 mm/1h, p<0,01, respectively). Patients with DXA had a longer cumulative prednisone exposure (5,42± 21,00 vs 1,14±7,58 months, p<0,001).
In the DXA group, we had 545 patients, with valid DXA data in 266 patients. The prevalence of osteoporosis was 16.5%. Patients with osteoporosis were older than patients without osteoporosis (55,89±13,95 vs 52,89±9,68 years, p<0,01). There was a positive association between BMD and body mass index, additionally, higher age was associated with lower BMD. The other variables, including the disease activity, showed no correlation with the BMD.
Conclusion: Our analysis shows that PsA patients from the SCQM register with higher osteoporosis risk (female patients, with elevated inflammatory parameters and longer prednisone exposure) were more likely to be scanned by DXA. Further research is needed to elucidate the association between PsA and osteoporosis.

P 14

Osteoporosis (OP) diagnosis and treatment of women aged ≥70 years in primary care: results from a large Europeal cross-sectional study

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Objective: To assess patterns of real-world OP diagnosis and medical treatment in European primary care.
Material and methods: Eligible patients were community-dwelling women aged ≥70 who visited their primary care physician for any reason and provided consent. Patient demographics, treatment history and clinical risk factors were collected via self-reported questionnaires and medical records. The primary objective was to assess the proportion of women aged ≥ 70 years at increased risk of fragility fracture and not receiving OP medication. Increased risk of fragility fracture was defined as at least one of (1) history of fracture, (2) 10-year probability of both hip and major OP fracture above country-specific FRAX thresholds, (3) T-score ≤ -2.5.
Results: 3798 patients (median age 77 years) were enrolled between Mar-Oct 2018 from 8 countries (Belgium, France, Germany, Ireland, Poland, Slovakia, Switzerland, UK). Visits were mainly for existing conditions (follow up for known disease 52.1%, medication refill 20.6%, new symptoms 21.7%). Prevalence of FRAX risk factors ranged from 1% (alcohol ≥3 units/day) to 32% (prior fracture). 2077 women (54.7%, median age 80 years) were determined to be at increased fracture risk, but only 30.9% of these had a recorded diagnosis of OP. For the primary outcome, 74.6% (95% CI: 72.7-76.5%) of women at increased risk of fragility fracture were not receiving any OP medication; this treatment gap was much lower in those with a recorded diagnosis of OP than in those without a recorded diagnosis (Figure). A small proportion of patients who did not meet the definition of increased risk for fragility fracture were diagnosed with OP (9.5%).
Conclusions: This real-world study of OP management in European primary care found that three-quarters of women aged ≥70 years at increased risk of fragility fracture were medically untreated for OP. Insufficient OP diagnosis appears to be an important barrier to treatment; future strategies need to increase awareness and facilitate the diagnosis of increased fracture risk to improve primary care management of OP.
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P 15

Association between the soluble terminal complement complex C5b-9 (sC5b-9) and signs of active kidney disease In a Swiss SLE cohort

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Background: A possible role of the terminal complement complex C5b-9 in active SLE has yet to be elucidated. Its proinflammatory effects on a number of cells types, e.g. glomerular mesangial cells and synovial fibroblasts, have been described.
Objective: To study whether sC5b-9 is associated with clinical disease activity in SLE and to compare it with C3, C4 and the split products C3a.
Methods
Study population and design: Patients from the Swiss SLE Cohort Study (SSCS, from St. Gallen centre, fulfilling the ACR criteria at inclusion), consecutively entered into a prospective observational study. Determined at two clinical visits, (≥ 6 months apart), compared with 18 healthy controls:
- clinical disease activity by clinical examination, SELENA-SLEDAI and SLICC Damage, SF-36, PGA, FACIT
- C3a and sC5b-9 by ELISA,
- standard of care routine laboratory parameters.

Statistics: Independent associations of continuous and categorical variables, studied by a mixed analysis of covariance (ANCOVA) models, followed by Spearman rank correlation analyses.
Results: 127 patients; age 51 ± 17 (mean ± SD) years (82% female), disease duration 5.8 [3.5-9.1] (median [IQR]) years. Initial clinical manifestations: arthritis (60%), hematologic (57%), photosensitivity (47%), skin changes (35%), oral ulcers (34%), renal disease (16%).
Lupus Low Disease Activity State in 87%, SELENA-SLEDAI (SLEDAI >0) of 49% (4.2 ± 3.1; mean ± SD).
IgG values were significantly associated with SELENA-SLEDAI (F = 4.94, p = 0.027) in a multivariate model, after adaptation for age, gender, CRP, ESR, ANA titre, dsDNA antibody value, complement factor C3 and C4.
Significant correlations /associations (univariate analyses) between:
1. sC5b-9 and haematuria (p<0.001)
2. sC5b-9 and glomerular dysmorphic erythrocytes (p = 0.020)
3. dsDNA ab and sC5b-9 (r = 0.221, p<0.001) with IgG (r = 0.421, p≤0,001)
4. C3a with sC5b-9 (r = 0.299, p≤0.001), C3a with C3 (r = 0.318, p = 0.01), C3a with C4 (r = 0.137, p = 0.02)

Sensitivities/specificities (with regard to haematuria and glomerular erythrocytes): sC5b-9: 75/63% and 64/62%; C3: 8/69% and 27/69%; C4: 8/84% and 18/84%.
A significant association of C3a with routine laboratory parameters of standard of care and of sC5b-9 with overall disease activity or other components of the SLEDAI, could not be detected.
Conclusions: Soluble C5b-9, elevated during haematuria and increased glomerular erythrocytes, could play a role in the pathogenesis of SLE and be useful as a marker of active renal disease.

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Severe myositis and perimyocarditis in anti-centromere positive systemic sclerosis complicated by thrombotic microangiopathy and renal insufficiency

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On February 2, a female patient (79 y) was admitted to the hospital after a collapse. She was hemodynamically stable, but tachypnoeic with bibasilar rales. She was not able to lift her arms over 45° or to sit in an upright position. There were facial and palmar teleangiectasia, digital ulcers, and skin thickening (face, forearms). In the echo, she had a diastolic dysfunction (I°,EF 60%) without regional motility alterations, but a pericardial effusion (1.1cm).
In her blood exams, a mild anemia, elevated muscle enzymes, cardiac biomarkers and CRP were detected (CK 3362 IU/L, CKMB 39 mcg/l, hsTrop 291pg/ml, NTproBNP 1367 pg/ml, CRP 24 mg/l).
Surprisingly, the high ANA titer of 1:10240 corresponded to positivity for anti–Centromere antibodies (abs) with absence of abs commonly associated with myopathy in systemic sclerosis (SSc) such as anti-Ku, anti-PM-Scl or anti-U1nRNP.
On MRI, signal intensity was mainly increased in the thighs and gluteal muscles, which corresponded to focal perivascular inflammation, MHC I upregulation besides chronic neurogenic changes on muscle biopsy.
We therefore postulated an overlap syndrome of polymyositis / SSc with perimyocarditis and initiated a therapy with solumedrol i.v. for 3 days, followed by prednisolone 1mg/kg bw and azathioprin. For the necrosis of the 5th digit, we started amlodipin and illoprost i.v.
Since at follow-up, muscle enzymes and cardiac biomarkers were still elevated (CK 2520, CKMB 69, hsTrop 490), we initiated treatment with IVIG (2g/kg bw) with good biochemical response (CK 1605). Despite having reduced the prednisolone dose rapidly below 10mg/d, slowly her renal function deteriorated without evidence of pre- or postrenal causes. Given the rise in blood pressure, we suspected scleroderma renal crisis and started the patient on increasing dosages of ACE inhibitors. Concurrently, her hemoglobin decreased and the parameter for hemolysis were positive (haptoglobin 0.13g/l) without evidence of an underlying primary hematologic disorder (dCoomps test neg. ADAMTS13 activity 82%) leading to the diagnosis of a SSc-associated thrombotic microangiopathy.
Herein, we describe an unusual case of an anti-Centromere positive SSc patient with severe inflammatory myopathy and perimyocarditis. This is in contrast to the currently available literature, which supports the absence of muscular involvement and the rarity of renal complications in this specific clinic-serologic subtype in the absence of diffuse cutaneous involvement.

P 17

An unexpected cause of a persistent inflammatory syndrome in a scleroderma patient

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Background: A persistent inflammatory syndrome in a patient with scleroderma can be a sign of ongoing disease activity, but can also have other causes, such as infection, neoplasia or amyloidosis.
The case: We present the case of a 59-year-old female patient with known limited cutaneous scleroderma. The manifestations at disease onset were dry eyes, arthritis, Raynaud, telangiectasia, livedo reticularis and puffy fingers. ACA and anti-PM-Scl100-Ab were positive. She was well controlled under Methotrexate (MTX) and Hydroxychloroquine (HCQ) with the exception of persistent inflammation (ESR 64 mm/1h, CRP 62 mg/l). A CT scan of neck, chest and abdomen showed no infection or neoplasia. There was no monoclonal gammopathy. She consulted for a routine examination at our clinic and reported an intentional 10 kg weight loss during the last year, abdominal cramps, loose stool and fatigue. The symptoms did not improve despite MTX-dose reduction. Liver enzymes were normal. A gastroscopy showed a H. pylori neg. gastritis and the colonoscopy showed two polyps. Three months later, despite an increased proton-pump inhibitor dose, symptoms persisted and lower limbs oedema with night sweats developed. The patient was hospitalized for further investigation. Echocardiography and ECG were normal, lung function tests showed a slightly diminished DLCO (74%). Renal function was normal, the low albumin level explained the leg oedema. We repeated the gastroscopy, and the histopathological analysis of the duodenum showed normal mucosa, but some PAS and Warthin-Starry positive macrophages in the submucosa without lymphocytic infiltrate. PCR for Tropheryma whipplei was positive in saliva, stool and duodenum biopsy-specimen. A treatment with Doxycycline was started and the HCQ-dosage was increased. The patient also received nutritional consultation. Two months later, leg oedema and night sweats improved and she gained weight, but she developed painful, erythematous nodules on the limbs and trunk. The MRI of the calves revealed an extensive fasciitis, interpreted as sign of immune reconstitution inflammatory syndrome treated with corticosteroids.
Conclusion: In case of persistent inflammatory syndrome with no apparent cause in a patient treated with immunosuppressive drugs, a Whipple disease should be suspected and searched for. There is no known association between Whipple disease and scleroderma, therefore we think that the presence of this two diseases in our patient was fortuitous.

P 18

Is very early systemic sclerosis a combination of mild and early?

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Background: SSc has a high morbidity and mortality, therefore it is important to detect the disease at an early stage. Very early detection of SSc allows early management, which has been shown to profoundly impact on the disease course in different inflammatory rheumatic diseases. However, patients fulfilling criteria for the diagnosis of very early SSc could also be patients with a very mild, very slowly progressing, long-standing disease.
Objectives: To identify a subgroup of patients with long-standing, very mild SSc among the patients fulfilling the criteria for the very early diagnosis of SSc by analyzing clinical, epidemiological and immunological characteristics of the Zurich patient cohort.
Methods: Baseline data of the SSc patients from the University Hospital of Zurich cohort are analyzed in this study. Demographic and disease characteristics of the patients enrolled between January 2009 and June 2018 into the Very Early Diagnosis of Systemic Sclerosis (VEDOSS) cohort were analyzed. Patients fulfilling the ACR/EULAR2013 criteria and patients with primary Raynaud phenomenon were excluded. Disease duration was calculated as the difference between the baseline visit date and the date of the first Raynaud's phenomenon (RP) symptom reported by the patient. For further analysis, the cohort was divided into two subgroups using a cut off value of </≥5 years disease duration. Data were expressed as absolute and relative frequencies (n/total valid cases (%)) and percentages for categorical variables or as means ± SD and medians ± interquartile range for continuous variables.
Results: A total of 107 patients met the inclusion criteria. Disease duration was 4 years (1, 10.25) and 100/107 (93.5%) of patients had RP. The majority of patients had a short disease duration measured from first Raynaud attack of <5 years. However, 43/107 patients (40.2%) had a long-standing disease with long-standing Raynaud`s. Further analysis of the clinical characteristics of early patients with </≥5years disease duration showed no significant differences in demographics and disease manifestations between the subgroups.
Conclusion: This analysis is showing that patients fulfilling VEDOSS criteria include a subgroup of patients with very mild, long-standing disease. This observation has major impact on the management of

VEDOSS patients, as this subgroup requires different follow up and treatment strategies compared to VEDOSS patients with early, progressive disease.

P 19

Nintedanib reduced decline in forced vital capacity across subgroups of patients with systemic sclerosis-associated interstitial lung disease: data from the SENSCIS® trial

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Background: In the SENSCIS® trial, nintedanib reduced the progression of interstitial lung disease associated with systemic sclerosis (SSc-ILD) compared with placebo, as demonstrated by a significantly lower rate of decline in forced vital capacity (FVC) over 52 weeks (primary endpoint).
Objectives: To assess the effect of nintedanib on the rate of decline in FVC in the SENSCIS® trial across pre-specified subgroups defined by baseline characteristics.
Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years before screening and ≥10% fibrosis of the lungs on a high-resolution computed tomography scan were randomised to receive nintedanib 150 mg twice-daily or placebo double-blind. The annual rate of decline in FVC (ml/year) assessed over 52 weeks (primary endpoint) was analysed in the overall population using a random coefficient regression model (with random slopes and intercepts) including anti-topoisomerase I antibody status, age, height, gender and baseline FVC as covariates and treatment-by-time and baseline-by-time interactions. Analyses in subgroups by baseline characteristics included terms for treatment-by-subgroup and treatment-by-subgroup-by-time interaction.
Results: A total of 576 patients were treated (288 in each group). Most (75.2%) of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years, and 21.4% of patients were aged ≥65 years. Generally, nintedanib had a consistent effect on reducing the rate of FVC decline across prespecified subgroups defined by baseline characteristics ($p>0.05$ for all treatment-by-time-by-subgroup interactions). The treatment effects estimates were comparable to the estimates of the primary analysis and the confidence intervals were overlapping. The analysis did not indicate a difference in the treatment effect of nintedanib across all subgroups assessed.
Conclusion: Nintedanib is effective at reducing ILD progression in a broad range of patients with SSc-ILD.

P 20

A novel device for fast minor salivary gland biopsy in suspected Sjögren's syndrome

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Background: Labial minor salivary glands (MSG) biopsies are a frequently performed diagnostic procedure for Sjögren's syndrome. MSG biopsy usually requires additional assistance e.g. to provide lower lip protrusion and to apply pressure on the lip during the procedure. The latter is done to foster protrusion of salivary glands and therefore to reduce the incision depth and potential nerve damage. We recently developed a new single-use device for MSG by 3D-printing in form of a lip clamp with a stamp on the lower arm to reduce invasiveness and to facilitate the intervention.
Objectives: To assess practicability and to describe the technical application of this device for MSG biopsies in the rheumatology department.
Methods: Retrospective study of MSG biopsies performed with the use of a dedicated lip clamp. For each MSG biopsy, we recorded if any assistance was needed during the procedure, occurrence of any complication, if salivary glands were obtained and if the quality of the salivary gland tissue sample was adequate for histologic analysis.
Results: 15 MSG biopsies were performed using the lip clamp on 15 patients with suspected Sjögren's syndrome between August 2018 and February 2019. Using the lip clamp, the physician was able to perform all the biopsies without assistance. No complication occurred with a follow-up of 1 week for each patient. Salivary glands tissue samples were obtained in 13/15 of the patients using 1 incision. For 2 patients, a second incision had to be performed on the contralateral side of the lip during the same intervention because no glands were found on the first attempt. Quality of all the samples was adequate for histologic analysis. From February to May 2019 the device was temporarily unavailable, and we performed 10 MSG biopsies with routine procedure (with the need of an assistant) and obtained salivary glands tissue samples in 9/10 of the patients. We did not observe differences in terms of procedure time between both techniques.
Conclusion: The use of a single-use lip clamp facilitates MSG biopsy without needing assistance and potentially reduces invasiveness and collateral damage. Quality of the tissue samples obtained was adequate for histological analysis.
Conflict of interest: AD: none, DD: none, BB: none, TH: has developed the device and holds rights.

P 21

Difficult to treat NXP2-positive polymyositis in a 38-year old woman

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Background: NXP2-positivity occurs in up to 25% of juvenile dermatomyositis (DM) patients. In adults, NXP-2 antibodies are rare, but possibly associated with malignancy.
Case report: A 38-year old woman was admitted to our ward with a creatin kinase of >18000 U/l. She had a 3 week-history of inflammatory pain and muscle weakness in the shoulder girdle, neck, and legs. The clinical examination showed a tetraparesis (M 3-4) without any specific dermal or joint features. The ANA titer was 1:640 without specific immunofluorescence pattern. NXP-2 positivity was detected by immunoblot. MRI confirmed myositis of the proximal upper and lower extremities. CT scan and echocardiography ruled out cardiopulmonary involvement. Nailfold capillaroscopy showed no organic microangiopathy. Extensive tumor screening was negative. Despite elevated troponin T and proBNP levels, cardiac MRI was normal. Muscle biopsy revealed no signs of a necrotizing myopathy, yet the perivascular inflammation and MHC-I upregulation seen was compatible with myositis.
Despite treatment with high dose corticosteroids, cyclophosphamide 1000 mg and rituximab 1000 mg iv, the patient was re-transferred from rehabilitation 2 weeks later with signs of acute, progressive cardiac decompensation and severe dysphagia due to affection of the pharyngolaryngeal musculature. Troponin T was substantially increased (75-fold for ULN) with only slightly elevated NTpro-BNP-levels. Echocardiography showed a good left-ventricular function and in the electrocardiogram no relevant arrhythmias were detected. However, now the cardiac MRI showed signs of myocarditis. Given these severe complications, the therapy was escalated with IVIG 2g/kg BW and the 2nd dose of rituximab 1000 mg iv. In addition, high doses of methylprednisolone were required for a prolonged period.
Discussion: While well known as a specific clinico-serologic subtype of juvenile DM, reports on NXP2-positive myositis in adults are extremely rare. According to the available literature, typical features in adults include a DM-phenotype with gastrointestinal involvement. Thus, we report a very unusual presentation of an NXP2-posititive polymyositis in an adult patient with severe cardiac and pharyngeal involvement with need for extended and combined immunosuppressive therapy. Our data support previous studies on the association of NXP2-positivity with poor prognosis in adults.

P 22

Evidence-based consensus for the identification and management of Interstitial lung disease in systemic sclerosis

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Background: Interstitial lung disease in systemic sclerosis (SSc-ILD) has high morbidity and mortality. There are no current guidelines for SSc-ILD screening, diagnosis and management to improve early detection and patient care.
Objectives: To develop expert consensus statements for SSc-ILD identification and management.
Methods: Based on a systematic literature analysis, evidence-based statements on SSc-ILD risk, screening, diagnosis, treatment and follow-up were developed. A modified Delphi process was used to establish SSc-ILD consensus statements. An expert panel, including 27 European-based pulmonologists, rheumatologists and internists, participated in online surveys, a face-to-face discussion and a WebEx meeting (Jul–Nov 2018). Panellists scored statements on a scale of 1 (strong disagreement) to 7 (strong agreement). Consensus was reached when ≥80% either disagreed (score: 1–3) or agreed (score: 5–7); statements that did not reach consensus were modified and re-voted on.
Results: The panel agreed on the following:
Risk factors: Presence of anti-topoisomerase I antibodies, male gender and diffuse cutaneous SSc increase ILD risk.
Screening: All SSc patients should have ILD screening by high-resolution computed tomography (HRCT) and lung function testing. HRCT screening frequency should be based on ILD risk and supplemented by clinical symptoms and lung function.
Diagnosis and assessment of severity: HRCT is recommended to diagnose SSc-ILD and assess severity, with support from lung function testing and clinical assessment.
Treatment initiation and options: All patients with severe or progressive SSc-ILD should be considered for pharmacological therapy (mycophenolate mofetil and cyclophosphamide are recommended). Those not receiving therapy should be followed for signs of disease progression.
Disease progression: Progression indicators include sustained lung function decline, worsening clinical symptoms and change in extent and/or pattern of fibrosis on HRCT.
Treatment escalation: Patients with inadequate treatment responses should be considered for treatment escalation. Lung transplant suitability should be evaluated early, especially in advanced disease. Autologous haematopoietic stem cell transplant may be considered in carefully selected patients.
Conclusion: These evidence-based expert consensus statements, developed using a modified Delphi process, provide important guidance for SSc-ILD identification and management.

P 23

Dermatomyositis bei einer 66-jährigen Patientin mit schwerem Hautbefall

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Dermatomyositis ist eine seltene Erkrankung mit einer Prävalenz von 6 bis 7 Fällen pro 100.000 Einwohner. Meist sind Frauen zwischen 40 bis 50 Jahren betroffen. Hier präsentieren wir den Fall einer 66-jährigen Patientin. Seit etwa 08/2018 wurde eine progrediente Rötung temporal beidseits, später im gesamten Gesicht, Hals und schliesslich auch am Rumpf, Armen und Beinen bemerkt. 09/2018 erfolgten zwei vergebliche Behandlungsversuche mit topischen Kortikosteroiden. Seit 12/2018 wurde eine Raynaud-Symptomatik und seit 01/2019 eine zunehmende Schmerzsymptomatik der Oberschenkel und Schultern beidseits bemerkt. Erwähnenswert ist ein Nikotinabusus mit 75 PY und ein Alkoholabusus. Klinisch imponierten neben dem ausgeprägten Exanthem ein Shawl Sign, Holster Sign und Gottronsche Papeln. An den Händen auffällig waren fleckige Hautrötungen mit Hyperkeratose, eine verminderte Rekapillarisationszeit und deutlich kalte Akren. Zusätzlich war eine schmerzlose PIP-Arthritis beidseits unverkennbar. Serologisch positiv waren antinukleäre Antikörper (1:640, fein granulär gesprenkelt) und SS-a/Ro p52, das Komplement C3 war erniedrigt. Die Hautbiopsie zeigte eine ausgeprägte vakuoläre Interface-Dermatitis mit epidermaler Atrophie und Ödem der papillären Dermis. Differentialdiagnostisch kam ein sekundäres Sjögren-Syndrom bei einem systemischen Lupus erythematodes in Frage. Die Diagnose einer Dermatomyositis wurde schliesslich von einem Dermatologen bestätigt. Eine erweiterte Diagnostik zum Ausschluss einer paraneoplastischen Problematik lehnte die Patientin ab. Zunächst wurde eine perorale Behandlung mit Prednison (20 mg/d bis 10 mg/d) ab Ende 02/2019 und danach eine Behandlung mit 15 mg Methotrexat subkutan wöchentlich begonnen. Ausserdem wurde eine Therapie mit Immunglobulinen geplant. Zusammenfassend ist festzustellen, dass die Diagnose einer seltenen Erkrankung häufig verzögert ist. Für das Krankheitsbild der Dermatomyositis sind ausreichend konklusive randomisierte Studien derzeit nicht verfügbar. Die Prognose ist von zusätzlichen viszeralen Beteiligungen (z. B. Lungen, Nieren, Malignität), Erhöhung der CK oder Serotypen abhängig.

P 24

Efficacy and safety of tocilizumab in patients with giant cell arteritis and visual disturbances

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Background: Giant cell arteritis (GCA) affects cranial arteries and may lead to visual impairment and blindness. Tocilizumab (TCZ) has recently been approved for treatment of GCA, however, data on its efficacy and safety in patients with initial visual affection is limited.
Objective: To study the outcome of patients with GCA and visual affection treated with TCZ.
Methods: We performed a retrospective single center study of all patients with GCA and visual impairment consecutively seen in our clinic between 4/2013 and 1/2019 who received TCZ.
Results: 16 GCA patients (13 women, 3 male) with a mean age of 76.3 + 9.7 yrs at GCA diagnosis and 25 affected eyes were treated with TCZ in addition to corticosteroids (CS). 2 patients experienced unilateral blindness while receiving iv pulse CS. AAION was diagnosed in 20/25 eyes, APION in 1/25 eyes and occlusion of the central retinal artery in 4/25 eyes. 14 patients were treated with TCZ iv 8mg/kg every 4 weeks, 2 patients received sc TCZ at 162mg every 2 weeks. All patients with visual symptoms received intravenous CS boluses, followed by prednisone 1mg/kg/day with subsequent tapering. Concomitant treatment consisted of low dose ASS in 11/16, oral anticoagulants in 5/16 and statins in 9/16 patients. Mean disease duration before initiation of TCZ was 3.8 + 5.7 months. 13/16 patients started with TCZ within 2 months after diagnosis of GCA, in 3 patients, TCZ was started because of refractory and/or relapsing disease. Mean follow-up time is 24 + 20.4 months in 5/2019.
Mean duration of TCZ therapy was 14.8 + 9.4 months. Mean duration on CS was 11.4 + 11.9 months. 9/16 patients stopped CS and have been steroid-free for a mean time of 14.7 + 8.3 months. 4/9 patients have discontinued TCZ and are drug-free at present for 8,13, 35 and 39 months. 2 additional patients were able to extent the infusion interval. 0/12 eyes with BCVA (best corrected visual acuity) <20/200 recovered, however, 6/9 eyes with baseline BCVA between 20/200 and 20/40 improved during TCZ. None of the patients with initial unilateral eye involvement, developed visual disturbances of the non-affected eye. Overall, TCZ was well tolerated. Vascular complications (TIA, aortic aneurysm, pulmonaly embolism) occurred in 3 patient. One patient died of concomitant cancer.
Conclusions: Although TCZ was unable to reverse unilateral blindness, no new visual symptoms occurred during or after TCZ treatment and the majority of patients were able to stop or reduce GC.

P 25

Long-term outcome of tocilizumab for patients with giant cell arteritis: Results from part 2 of the GiACTA trial

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Introduction: Tocilizumab (TCZ) 162 mg administered SC weekly (QW) or every-other-week (Q2W) plus 26-week prednisone tapering resulted in higher rates of sustained glucocorticoid (GC)–free remission in patients (pts) with giant cell arteritis (GCA) than placebo plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering in the 52-week, double-blind, randomized controlled GiACTA trial. We here analyzed long-term safety and maintenance of efficacy in GCA pts in a 2-year long-term extension (part 2) of this trial.
Methods: After 52 weeks, pts in clinical remission (CR, absence of flare per investigator assessment) stopped TCZ treatment upon entering part 2. Subsequent GCA therapy, including initiation/termination of open-label TCZ and/or GC, was at the investigator's discretion. Outcomes included maintenance of CR (no flare during part 2), flare, time to first flare, treatments received, cumulative GC dose, and safety. Treatment groups refer to originally assigned treatment (PBO or TCZ).
Results: 215/250 pts entered part 2 and 92% completed 3 years in the trial. 38/81 (47%) TCZ QW and 13/36 (36%) TCZ Q2W pts maintained CR during part 2. Of these, more pts (65%) were treatment-free (no TCZ and GC) vs original PBO pts (45%), with the highest proportion in the TCZ QW group (66%). Median time to first flare without TCZ was longer for pts in the original TCZ groups (TCZ QW, 575 days; TCZ Q2W, 428 days) than in the original PBO groups (PBO+26, 162 days; PBO+52, 295 days); TCZ QW patients remained flare-free the longest. Retreatment with TCZ effectively restored CR in part 2. Cumulative 3-year GC dose was lowest in the TCZ QW group (median dose [mg/day]: TCZ QW, 2372.8; TCZ Q2W, 2863.0; PBO+26, 5006.0; PBO+52, 5322.5). Rates of serious adverse events per 100 patient-years over 3 years were comparable for pts never receiving TCZ (23.2) and receiving ≥1 dose of TCZ (25.4).
Conclusion: Nearly half the pts treated with TCZ QW maintained CR throughout part 2, though flares still occurred in the remaining pts once they discontinued TCZ treatment. Retreatment with TCZ restored CR in patients who experienced flare. Among pts maintaining CR in part 2, higher proportions of pts originally assigned to TCZ were treatment-free compared with those originally assigned to PBO. Cumulative GC doses over 3 years were lowest in patients originally assigned to TCZ. No new safety signals were observed with TCZ exposure in GCA pts during the 3-year study.

P 26

A case of erythema induratum of Bazin with aortitis and arthritis

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We describe a 27-year old woman of Asian descent who spends her holidays in the Philippines. From the age of 4, she started having recurrent ulcerating nodules on her legs that regress spontaneously leaving hyperpigmented scars. It was initially treated as streptococcal skin infection.
She was seen by a dermatologist in 2006 and a possible diagnosis of erythema induratum of Bazin was made. However, the patient was lost to follow-up. She started having swollen and painful ankle and was then seen by a rheumatologist in 2011. The arthrocentesis and synovial fluid analysis revealed inflammatory arthritis. Due to the persistence of the above symptoms, she was seen by a second dermatologist in 2016 and further diagnostic tests were done. CT of the chest and abdomen revealed mesenteric and inguinal lymphadenopathy with inflammatory thoracic aorta aneurysms. Due to her asian ancestry together with the radiologic signs of vasculitis and arthritis, she was seen in the rheumatology department for further evaluation. Joint fluid culture and PCR for MTB were both negative. Other form of autoimmune arthritis and connective tissue diseases were ruled out by appropriate investigations. Histology reveals necrotizing granulomatous lymphadenitis and PCR was positive for Mycobacterium tuberculosis. Thus the diagnosis of erythema induratum of Bazin was made and treatment with quadruple anti-tuberculosis treatment was started. In the light of the tuberculosis infections, the vasculitis was interpreted as infectious in nature. This was later confirmed histologically when she underwent aortic replacement surgery in December 2017.
Tuberculosis is still a current disease with both pulmonary and rare extra-pulmonary manifestations that can mimic an autoimmune disease. In this case, we showed 3 rare extra-pulmonary manifestations of tuberculosis: erythema induratum of Bazin, Poncet's arthritis and tubercular aortitis.

P 27

Off-label use of rituximab in rheumatic diseases, a swiss tertiary centre experience

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Background: Rituximab (RTX) is licenced for the treatment of rheumatoid arthritis (RA) and ANCA-associated vasculitis. RTX is frequently used off-label to treat other auto-immune diseases (AID), especially connective tissue diseases (CTD). There are no published data about off-label use of RTX in AID in Switzerland.
Objectives: To describe off-label use of RTX in a real-life setting, when treating AID.
Methods: Retrospective cohort study of all patients treated with RTX in the Rheumatology Department between 2005 and 2017. Clinical efficacy of RTX after 12 and 24 months of treatment was classified as no response (NR), partial (PR) and complete response (CR). RTX discontinuation rate was analysed using Kaplan-Meier method. Occurrence of serious adverse events (SAE) and anti-RTX antibodies (ADA) were reported.
Results: 167 patients treated with RTX were identified: 29% for CTD, 62% for RA and 9% for other AID. RTX was used off-label in 74% of the patients according to Swiss official indications. No significant differences in terms of clinical response were observed between off-label and in-label use after 12 months (NR: 16%/14%, PR:49%/48%, CR:36%/38%, n = 103/29, p = 0.97) and 24 months (NR:13%/10%, PR:38%/30%, CR:49%/60%, n = 76/20, p = 0.67), respectively. Clinical response after RTX treatment did not differ significantly between patients with CTD and RA after 12 months (NR:10%/13%, PR:50%/51%, CR:40%/36%, n = 42/78, p = 0.81) and 24 months (NR:7%/10%, PR:32%/44%, CR:61%/46%, n = 28/59, p = 0.43), respectively. Survival curves of RTX treatment from CTD group closely matched that from RA group (HR 0.91 95% CI 0.61-1.38). Causes of RTX treatment discontinuation in patients with CTD (n = 26) and RA (n = 65) consisted of lack of efficiency (62%/55%), adverse event (19%/34%) and remission (19%/11%, p = 0.3).
SAE (n = 108) occurred in 34% of the patients and consisted of infectious SAE (43%) and perfusion-related AE (6%). 13%/22% of the patients with CTD/RA (n = 47/103) presented at least one infectious SAE (p = 0.15). 5 patients with RA and 3 patients with CTD died during RTX treatment. Low IgG levels were observed in 33% (46/141) of the patients graded as mild (21%), moderate (10%) or severe (2%). ADA were observed in 6/43 patients.
Conclusion: Efficacy of RTX was similar in off-label vs. in-label use. RTX discontinuation rate was comparable in patients treated for CTD and RA in our population. Patients with RA were more prone to undergo adverse events by RTX than patients with CTD.

P 28

This poster was retracted.

P 29

Efficacy of apremilast for oral ulcers associated with active Behçet's syndrome over 64 weeks: results from a phase III study

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The RELIEF study assessed apremilast (APR) efficacy and safety for oral ulcers (OU) associated with Behçet's syndrome, a chronic disorder characterized by recurrent OU that can impact quality of life (QoL). Adult patients (pts) with active Behçet's syndrome (≥3 OU at randomization or ≥2 OU at screening and randomization without active major organ involvement) were randomized (1:1) to placebo (PBO) or APR 30 mg twice daily for 12 wks and then continued APR (APR/APR) or switched from PBO to APR (PBO/APR) through Wk 64. Pts then entered a 4-wk posttreatment observational follow-up. The primary endpoint, area under the curve for the number of OU over 12 wks (AUCWk0-12), reflects the number of OU over time and accounts for the recurring-remitting course of OU. Change from baseline in OU pain visual analogue scale, complete response (% of pts with no OU), partial response (% of pts with ≥50% reduction in OU count), disease activity (Behçet's Disease Current Activity Form, comprising the Behçet's Disease Current Activity Index [BDCAI], Pt's and Clinician's Perception of Disease Activity and Behçet's Syndrome Activity Score [BSAS]) and QoL (Behçet's Disease QoL [BDQoL]) were assessed. Of 207 pts randomized and receiving ≥1 dose of study medication (PBO: n = 103; APR: n = 104), 178 entered the active treatment phase (PBO/APR: n = 83; APR/APR: n = 95); 143 pts (PBO/APR: n = 68; APR/APR: n = 75) completed Wk 64. AUCWk0-12 was significantly lower with APR vs PBO (LS mean difference [95% CI]: −92.6 [−130.6, −54.6]; P<0.0001). Significantly lower OU counts (P≤0.0015) and greater improvement from baseline in OU pain (P≤0.0035) were observed with APR vs PBO each wk from Wks 1-12, and the efficacy of APR was sustained up to 64 wks. Significantly more pts achieved complete and partial response of OU at Wk 12 with APR vs PBO (P<0.0001); effects were maintained through Wk 64 in APR/APR pts who remained in the study (complete response: 53.3%; partial response: 76.0%). Improvements in BDCAI (P = 0.0335), BSAS (P<0.0001) and BDQoL (P = 0.0003) were significant with APR vs PBO at Wk 12 and maintained at Wk 64. Improvements decreased within 4 wks of APR discontinuation. The most common adverse events with APR were diarrhoea, nausea, headache and upper respiratory tract infection; no new safety concerns emerged. APR demonstrated efficacy in OU in pts with active Behçet's syndrome that was sustained up to 64 wks with continued treatment. Safety was consistent with APR's known profile.

P 30

Site-specific effectiveness of TNF inhibitors for enthesitis in DMARD-naive patients with axial spondyloarthritis

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Background: Enthesitis is a hallmark of spondyloarthritis (SpA), with substantial impact on quality of life. Although pathophysiological mechanisms of enthesitis may include both mechanical and autoimmune features, improvements upon initiation of TNF-inhibitors (TNFi) across individual enthesitis sites have not been reported in real-world patients with axial SpA (axSpA).
Objectives: To investigate the effectiveness of TNFi in axSpA patients without prior DMARD treatment at specific enthesitis sites.
Methods Retrospective cohort study using the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry. AxSpA patients initiating TNFi without previous DMARD (biologic or conventional synthetic DMARD [csDMARD]) use and with available Maastricht Ankylosing Spondylitis Enthesitis Score, modified to include the plantar fascia, (MASES) at start of treatment ('BL') and after 6 months (± 3 months [mo]) of follow up (FU) were included. Presence of enthesitis was defined as at least 1 inflamed enthesis. Among patients (pts) with any enthesitis present at BL, #pts with enthesitis at each MASES site was assessed at BL & 6mo FU. Fisher's exact test was used to assess significant enthesitis resolution at each enthesitis site between BL & 6-mo FU.
Results 781 DMARD-naive pts with axSpA who initiated TNFi were identified. At BL, pts (57% male) were a median of 40 (interquartile range [IQR]) = 31-50) years of age with a median disease duration of 9 (IQR = 3-18) years and median Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) of 3.4 (IQR = 2.8-3.9) at treatment initiation. A subgroup of 160 TNFi pts had active enthesitis at BL (MASES: mean = 4.14, sd = 2.87) and a 6-mo FU visit with MASES available (MASES: mean = 2.07, sd = 2.82), with a mean MASES reduction at the FU visit of 2.07 (sd = 3.06). At the 6-mo FU, complete enthesitis resolution was observed for 72 (45.0%) of pts. Enthesitis resolution was most frequent at the following sites: the costochondral sternum, the costochondral joint, the lumbar vertebra, the pelvic crest, and spina iliaca posterior.
Conclusion: Our results suggest that for real-world DMARD-naïve axSpA pts, TNFi are generally effective for resolving enthesitis. Significant resolution was observed for enthesitis of the spine and thoracic cage though resolution was more limited for plantar fascia or Achilles tendon enthesitis. Lower limb entheses are more prone to mechanical strain and may therefore require alternative or more prolonged therapy.

P 31

Ixekizumab significantly improves signs, symptoms and spinal inflammation of active ankylosing spondylitis/radiographic axial spondyloarthritis: 16-week results of a phase 3 randomised, active and placebo-controlled trial

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Background/Purpose: COAST-V is the first Phase 3 study of ixekizumab (IXE), a high-affinity anti-IL-17A monoclonal antibody, in bDMARD-naive patients with active radiographic axial spondyloarthritis (r-axSpA).
Methods: Adults with active r-axSpA per Assessment of SpA international Society (ASAS) criteria (sacroiliitis centrally defined by modified New York Criteria and ≥1 SpA feature), BASDAI ≥4, back pain ≥4 and inadequate response or intolerance to NSAID therapy, were randomised 1:1:1:1 to subcutaneous placebo (PBO), 80 mg IXE every 4 (Q4W) or 2 (Q2W) wks, with either 80-mg or 160-mg starting dose (assigned 1:1), or 40 mg adalimumab (ADA) Q2W (active reference arm) up to Wk 16. The primary endpoint was ASAS40 response at Wk 16. Major secondary endpoints included ASAS20, BASDAI50 and change from baseline (CFB) in MRI spine and sacroiliac joint SpA Research Consortium of Canada (SPARCC) scores (all images were centrally read). In addition, the CFB is reported for high sensitivity C-reactive protein (hs-CRP) and the 4 patient domains used for calculation of the ASAS response: patient's global assessment (PGA), BASFI, spinal pain and BASDAI stiffness. Categorical endpoints were analysed by logistic regression with non-responder imputation for missing data. Continuous endpoints were analysed by a mixed-effects model of repeated measures. Safety was assessed.
Results: Of 341 subjects randomised, 97% completed Wk 16. Their mean age was 41.7 years; mean time since r-axSpA symptoms onset was 16.0 years, and mean BASDAI was 6.7. At Wk 16, significantly higher proportions of IXE-treated patients achieved ASAS40, ASAS20 and BASDAI50 vs PBO. Compared with PBO, both IXE regimens had significantly higher CFB improvements in MRI spinal and sacroiliac joint inflammation and hs-CRP at Wk 16 and, as early as Wk 1, significant CFB improvements in all ASAS components. At Wk 16, ADA showed significant improvements vs PBO for ASAS40 and for PGA, BASFI, NRS spinal pain and BASDAI stiffness CFB. There was one opportunistic infection (Candida infection, ADA arm), one case of inflammatory bowel disease (IXEQ2W arm) and no malignancies or deaths.

Conclusion: The primary and all major secondary endpoints for IXE were met at Wk 16 with no unexpected safety findings. IXE was superior to PBO for improving r-axSpA signs and symptoms and objective signs of inflammation.

P 32

Sustained improvements in disease activity for up to two-years with ixekizumab in patients with active psoriatic arthritis who were either biologic-naïve or with previous inadequate response to tumour necrosis factor inhibitor therapy

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Background: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets IL-17A and is approved for the treatment of psoriatic arthritis (PsA). The efficacy and safety of IXE 80mg every 4 weeks over two years of treatment in patients who were either biologic disease-modifying antirheumatic drug (bDMARD) naïve or tumour necrosis factor inhibitor inadequate responders (TNF-IRs) are presented.
Methods: Data were analysed from two double-blind, placebo (PBO)-controlled, Phase III trials. Patients with active PsA who were bDMARD-naïve (SPIRIT-P1) or TNF-IR (SPIRIT-P2) were randomised to PBO, IXE 80mg every 4 weeks (IXEQ4W) or IXE 80mg every 2 weeks (IXEQ2W) (after a 160mg starting dose for both IXE Q4W and IXE Q2W or adalimumab (ADA) 40mg Q2W in SPIRIT-P1). At week 16, non-responder patients received rescue therapy. At week 24, any patients on PBO (or ADA in SPIRIT-P1) were re-randomised to IXEQ2W or IXEQ4W. Efficacy measures included American College of Rheumatology (ACR) 20/50/70 responses, Psoriasis Area and Severity Index (PASI) 75/90/100 responses, Leeds Enthesitis Index (LEI), Leeds Dactylitis Index-Basic (LDI-B), Health Assessment Questionnaire Disability Index (HAQ-DI) score, Minimal Disease Activity (MDA) and Nail Psoriasis Severity Index (NAPSI) score. Missing values were imputed by modified nonresponder imputation (mNRI) for categorical data or modified baseline observation carried forward (mBOCF) for continuous data. Safety analyses included patients receiving ≥1 dose of IXE.
Results: At week 108, patients treated with IXEQ4W demonstrated sustained improvements in ACR20/50/70, PASI 75/90/100, NAPSI responses, resolution in LEI and LDI-B, and improvements from baseline in HAQ-DI. Data from SPIRIT-P1 and SPIRIT-P2 also showed sustained improvement (change from baseline) in fatigue NRS (IXEQ4W: mean change± standard deviation: -1.9±2.7 and -1.8±2.8, respectively). Efficacy and safety results of IXEQ4W were consistent with 24- and 52-week results from SPIRIT-P1 and SPIRIT-P2. No new safety signals were reported.
Conclusion: IXE provided clinically meaningful and sustained improvements in the major clinical domains of PsA for up to two years of treatment, among patients who were either biologic-naïve or with prior inadequate response or intolerance to TNFi. No unexpected safety signals were reported.

P 33

Earlier treatment of non-radiographic axial spondyloarthritis with certolizumab pegol results in improved clinical outcomes

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Background: Axial spondyloarthritis (axSpA) diagnosis is often delayed, which leads to treatment (Tx) delay.1 Certolizumab pegol (CZP) can improve signs and symptoms of non-radiographic (nr)-axSpA,2 but whether earlier CZP Tx is beneficial in these patients (pts) is unclear. We report clinical outcomes in pts with nr?axSpA treated with CZP or placebo (PBO) over 52 weeks (wks), by symptom duration.
Methods: Post-hoc analyses of disease outcomes in pts stratified by symptom duration (<5 vs ≥5 yrs at baseline [BL]) from C-axSpAnd (NCT02552212) were performed. In this 52?week, phase 3, multicentre, double-blind, PBO-controlled study, pts were randomised 1:1 to PBO or CZP (400mg at Wks 0/2/4, then 200mg every 2 wks). Pts could adjust non-biologic background medication or switch to open-label biologics at any point.2 Outcomes reported include responder rates for Ankylosing Spondylitis Disease Activity Score – major improvement (ASDAS-MI; reduction ≥2.0/lowest score [0.6]), ASAS 40% improvement (ASAS40) and ASAS partial remission (ASAS-PR; ≤2 in all domains); proportion of pts who reached ASDAS-inactive/low disease (ASDAS-ID [<1.3]/LD [≥1.3 <2.1]) or ASDAS<2.1; and change from BL (CFB) in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Missing values were imputed using non-responder imputation (NRI; categorical measures) or last observation carried forward (LOCF; quantitative measures).
Results: Of 317 recruited pts, 159 were randomised to CZP, and 158 to PBO. Mean (standard deviation [SD]) BL symptom duration was 7.8 (7.7) yrs for CZP-treated pts and 8.0 (7.5) yrs for PBO pts. 50.3% (80/159) CZP pts and 48.7% (77/158) PBO pts had a symptom duration <5 yrs. At Wk52, CZP-treated pts with shorter symptom duration (<5 yrs vs ≥5 yrs) had substantially better responder rates for ASDAS-MI (55.5% [n = 44] vs 39.2% [n = 31]), ASAS40 (65.0% [n = 52] vs 48.1% [n = 38]) and ASAS-PR (43.8% [n = 35] vs 24.1% [n = 19]; all NRI). Similarly, more pts with symptoms <5 yrs reached ASDAS-ID (40.5% [n = 32] vs 17.9% [n = 14]) and ASDAS<2.1 (65.8% [n = 52] vs 52.6% [n = 41]; both LOCF). PBO pts had low response rates and no consistent trends in outcomes by symptom duration.
Conclusion: CZP-treated nr-axSpA pts with shorter symptom duration (<5 vs ≥5 yrs) showed greater improvements across multiple signs and symptoms of disease. Early CZP Tx may be beneficial to nr-axSpA pts.
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P 34

Rapid and sustained improvements in patient-reported outcomes with ixekizumab in biologic-naïve and TNF-inadequate responder patients with psoriatic arthritis

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A, has shown improvements in sign and symptoms of psoriatic arthritis (PsA) in patients who were biologic naïve and in patients who failed prior TNF-inhibitors (TNFi-inadequate responders [IR]). Here, we report the onset and duration of IXE treatment effect on patient-reported outcomes (PROs).
Methods: The PROs data were taken from two phase-3 trials: SPIRIT-P1 (Population-bDMARDs naïve) and SPIRIT-P2 (TNFi-IR). Randomised patients received IXE 80 mg every 2 weeks (Q2W) and every 4 weeks (Q4W) after 160 mg initial dose, or placebo. The following PROs were assessed from baseline up to 108 weeks: Joint pain visual analog scale (VAS), patient global assessment (PatGA), fatigue numerical rating scale (NRS), and health assessment questionnaire- disability index (HAQ-DI).
Results: Patients treated with IXE Q4W dose in SPIRIT-P1 and -P2 studies reported rapid (as early as week 1) and consistent improvement in PROs throughout 52 weeks. Long-term treatment until week 108 with IXE showed sustained improvement in PROs in SPIRIT-P1 and -P2 studies, with mean change (±standard deviation) from baseline (IXEQ4W) in fatigue NRS (-1.9±2.7 and -1.8±2.8) and HAQ-DI (-0.6±0.5 and -0.4±0.6), respectively. Safety profile of IXE in patients with PsA is consistent with previously reported safety results from pooled data of phase 3 trials and no new safety signals were identified with longer IXE treatment exposure.
Conclusion: These data demonstrate that patients with PsA treated with IXE achieve rapid and sustained improvements in PROs irrespective of prior biologic exposure.

P 35

Efficacy and safety of ixekizumab in the treatment of radiographic axial spondyloarthritis: 16 week results of a phase 3 randomised, double-blind, placebo-controlled trial in patients with prior inadequate response or intolerance to 1 or 2 tumour necrosis factor inhibitors

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Background: TNFi are recommended for patients with axSpA who do not respond to or tolerate NSAIDs. axSpA patients with inadequate response (IR) or intolerance to TNFi have not been exclusively studied in a clinical trial. In COAST-W (NCT02696798), we investigated the efficacy and safety of ixekizumab, a high-affinity monoclonal antibody that selectively targets IL-17A, in patients with active radiographic axSpA (r-axSpA) with prior use to 1 or 2 TNFi.
Methods: In this randomised, double-blind, placebo-controlled, Phase 3 trial, adult patients with IR/intolerance to 1 or 2 TNFi and an established diagnosis of r-axSpA (patients fulfilling ASAS classification criteria for axSpA, with radiographic sacroiliitis centrally defined by modified New York criteria) were recruited and randomised 1:1:1 to placebo (PBO) or 80-mg subcutaneous ixekizumab every 2 (IXEQ2W) or 4 (IXEQ4W) weeks (wks), with either 80-mg or 160-mg starting dose (assigned 1:1). The primary endpoint was ASAS40 response rate at Wk16. Secondary endpoints included CFB in MRI spine and sacroiliac joint SPARCC scores. In addition, the CFB is reported for hs-CRP and the 4 patient domains used for calculation of the ASAS response: PGA, BASFI, spinal pain and BASDAI stiffness. Categorical outcomes were analysed by logistic regression with non-responder imputation. Continuous outcomes were analysed by mixed-effects model of repeated measures except MRI SPARCC scores (ANCOVA using observed case). Safety was assessed.
Results: 316 patients were randomised to PBO (N = 104), IXEQ2W (N = 98) or IXEQ4W (N = 114). All patients possessed very active (mean BASDAI: 7.4±1.3) and long-standing disease (median duration of symptoms = 16.7 years); 90% had a prior IR and 10% were intolerant to TNFi. At Wk16, ASAS40 was significant with IXE [IXEQ4W = 25.4%; IXEQ2W = 30.6%] compared to PBO [12.5%]. Compared with PBO, IXE-treated patients showed significantly greater CFB in secondary endpoints including PGA, spinal pain and BASDAI stiffness, spinal MRI and SIJ inflammation, and high sensitivity CRP, at Wk16 and, as early as Wk1. Most TEAEs were mild/moderate. Serious AEs were consistent across arms. One death was reported (IXEQ2W) due to suicide which was not attributable to study drug per the blinded principal investigator.
Conclusion: The primary and all major secondary endpoints for IXE were met at Wk16 in patients with previous IR or intolerance to one or two TNFi, compared to PBO.

P 36

Efficacy and safety outcomes in patients with axial spondyloarthritis treated with certolizumab pegol: results from the 48-week run-in part of C-OPTIMISE

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Background: C-OPTIMISE is the first trial to evaluate whether certolizumab pegol (CZP) can be reduced/discontinued in patients with radiographic(r)-axSpA/ankylosing spondylitis (AS) and non-radiographic(nr)-axSpA achieving sustained remission after 48 weeks' (wks') treatment. We report interim efficacy and safety data for both axSpA subpopulations from the C-OPTIMISE trial.
Methods: C-OPTIMISE (NCT02505542) was open-label to Wk48 (Part A), followed by 48-wk parallel-group, double-blind, placebo-controlled treatment (full dose and half dose) to Wk96 (Part B). Patients with adult-onset axSpA of <5 years' duration, fulfilling ASAS classification criteria, were recruited. In Part A, patients received CZP 400mg at wks0/2/4, then 200mg every 2 weeks (Q2W). Patients achieving sustained remission in Part A (ASDAS<1.3 at Wk32 and <2.1 at Wk36 [or vice versa], and <1.3 at Wk48) were eligible for Part B (secondary outcome). The primary outcome was the percentage of patients in Part B not experiencing a flare (not reported here). Missing values were imputed using non-responder imputation (NRI) or last observation carried forward (LOCF).
Results: A total of 736 patients were recruited in Part A (r-axSpA/AS: n = 407; nr-axSpA: n = 329). Mean (SD) time since diagnosis was 2.2 (1.7) years (r-axSpA/AS: 2.5 [1.8]; nr-axSpA: 1.8 [1.6]). At baseline, 98.5% patients had high/very high disease activity (ASDAS≥2.1); at Wk48, 52.7% (r-axSpA/AS: 52.6%; nr-axSpA: 52.9%) had inactive disease (ASDAS<1.3; LOCF). Of 736 patients, 43.9% achieved sustained remission (r-axSpA/AS: 42.8%; nr-axSpA: 45.3%; NRI). The treatment-emergent adverse event (TEAE) rate was 224.2/100 patient-years' exposure; 4.5% patients discontinued CZP due to TEAEs. No new safety signals were identified.
Conclusion: The run-in phase of C-OPTIMISE shows that similar and substantial proportions of patients with r-axSpA/AS and nr-axSpA achieved sustained remission during 48 wks' CZP treatment. No new safety signals were identified.

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Comparative effectiveness research in observational settings: evaluating two new methods to analyse response rates

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Background: Comparing response rate (rr%) in observational studies is hampered by two major threats.
1. Confounding: Patient, disease, and treatment characteristics often differ for each drug.
2. Attrition bias: Assessing %rr after a set time excludes patients who discontinued their treatment, which may overestimate drug effectiveness.
Objectives: Propose two new methods (3 and 4) to compare %rr in patients with different baseline characteristics, while accounting for attrition and compare them to established methods (1 and 2).
Sample
Illustration using CDAI low disease activity (≤10) rates in data from a collaboration of registries1 with 3448 patients treated by a biologic, either intravenously (IV: n = 2414) or subcutaneously (SC: n = 1034).
Methods
1. Complete case (CC)
   %rr is computed as the percentage of responders on total patients still on treatment at the given time point.
2. LUNDEX2:
   CC %rr is corrected for attrition by multiplying it by the Kaplan Meier estimates of the survival (SKM), thus considering all patients not on treatment as non-responders, irrespective of the reason for drug discontinuation.
3. Propensity Score Matching LUNDEX (PSM LUNDEX)
   A: Select patients in both exposure groups using propensity score matching
   B: Use the LUNDEX to compute the %rr.
4. Confounder-Adjusted Response Rate with Attrition Correction by reason for drug discontinuation (CARRAC)
   A: Compute estimates of drug survival for the main reasons of drug discontinuation (e.g., ineffectiveness, adverse events).
   B: Estimate %rr using random effect IPD meta-analysis with estimates for each reason of drug discontinuation.

C: Combine %rr estimates using weights of step A.
Results: Compared to CC analysis, differences in %rr between the SC and IV groups were smaller for the LUNDEX methods, larger for PSM LUNDEX, and close to CC for the CARRAC method. For PSM LUNDEX, overlapping propensity score only allowed to select 561 patients per group.
Conclusion: Both LUNDEX methods may underestimate the true response rates by considering all patients stopping treatment as non-responders, while complete case method may overestimate the %rr by considering patients stopping as having a similar %rr to patients continuing treatment. The CARRAC method, which accounts for attrition by reason for drug discontinuation, obtained %rr estimates in between complete-case and LUNDEX corrections. Simulations studies are needed to evaluate the best method.

References:
1 Lauper et al. 2018 RMD Open
2 Kristensen et al. 2006 A&R

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An atypical chest pain

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A 50 years old man presented to the emergency departement with widespread pain, especially at chest level, fever and night sweats. He refers fever with stakes up to 39 ° C in the two days prior to hospitalization at the Department of Rheumatology.
Physical examinations revealed a swelling with localized pain in the left sternoclavicular joint. Laboratory tests showed a CPR of 134 mg/l and a ESR of 70 mm/h. Uric acid is within the norm (263 mmol / l).
The patient's anamnesis is for a chronic gouty arthritis characterized by the presence of tophi and frequent arthritis, a type 2 diabetes poorly controlled, a lumbosacral radicular syndrome irritative L3 on the left side and obesity that is why he underwent a gastric banding surgery. Social history: the patient declares drinking 2-3 liters of carbonated soft drinks a day.
Home therapy: Metformin, Sitagliptin, Gliclazide, Naproxen with partial benefit on pain and Febuxostat.
Differential diagnoses of sternoclavicular swelling includes infectious, crystals or psoriatic arthropathy, Tumor pathology, SAPHO syndrome.
An ultrasound scan performed at thoracic level showed the presence of effusion in the sternoclavicular joint. A thoraco-abdominal CT scan, performed in doubt of neoplasias, shows no masses but osteo structural nonspecific alterations of the sternoclavicular joint. We performed a Dual energy CT (DECT) which report a gouty arthropathy at the sternoclavicular joints (in the literature only three similar cases are proved).
Because of the poor therapeutic effects using Febuxostat and systemic corticosteroids, the patient was treated with Anakinra, an interleukin 1 receptor antagonist, which led, 6 months after the event, to a total remission.

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Rheumatology from A to Z – a web-based information tool

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Online health information is frequently consulted. However, appropriately examining this data for its quality, trustworthiness, and clinical relevance presents a challenge even for medical professionals. This project offers content in the areas of the musculoskeletal system that has been compiled and verified by experts. Overall, 222 terms are defined, explained and equipped with clinically relevant details in order to provide interested professionals with quick and encompassing access to high-quality, subject-specific information. In addition, these terms are supplemented with a total of 2150 links to websites of verified quality with further information. All content is provided in English and German and can be retrieved either by website or by app.

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Preclinical evaluation of targeting TGF-beta signaling and senescence in ex vivo models of human knee and spine osteoarthritis

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Background & purpose: The absence of effective disease-modifying drugs remains an important unmet need in the treatment of osteoarthritis. In recent years, novel pharmacological treatments including targeting TGF-beta signaling in subchondral bone (Zhen et al., Nat Med 2013) or senescence of joint tissues (Jeon et al., Nat Med 2017) have demonstrated promising efficacy in experimental osteoarthritis. However, the translation from experimental models to humans has not been pursued to date. Here, we determined therapeutic and deleterious side effects of these treatment strategies in a preclinical explant model of human knee and facet joint osteoarthritis.

Methods: Osteochondral tissue explants of osteoarthritic human knee tibial plateaus (n = 10) or lumbar facet joints (n = 10) were cultured for one week in the presence and absence of an inflammatory stimulus (1 µg/mL LPS). Specimens were left untreated (control) or treated with a senolytic agent (4.5 mg/mL quercetin) or inhibitor of TGF-beta receptor signaling (10µm SB-505124). Subchondral bone turnover (Pro-Collagen-Iα) and tissue infl ammation (IL-6, MCP-1) was assessed by ELISA.
Results: Explanted tissues showed no appreciable loss of viability during culture and drug treatment. LPS challenge led to a 4- and 3-fold induction of IL-6 and MCP-1 tissue secretion, respectively. Subchondral bone turnover was not affected by inflammatory conditions. The therapeutic effect of TGF-beta signaling inhibition was revealed by a drastic reduction of pro-Col-I (~75%) and IL-6 (~50%) secretion. Unexpectedly, MCP-1 secretion was significantly elevated (~200%) revealing a TGF-beta-dependent negative feedback mechanism. This side effect was specific for knee osteoarthritis and not observed in facet joint specimens. Senolytic treatment with quercetin did not affect bone turnover, yet strongly induced IL-6 tissue secr etion under control (~400%) and inflammatory conditions (~200%).
Conclusion: Taking advantage of a preclinical model of human osteoarthritis, we established therapeutic efficacy of TGF-beta signaling inhibition on subchondral bone turnover in knee and spine. Elevated MCP-1 secretion upon TGF-beta targeting and increased tissue inflammation using senolytic drugs prompt careful evaluation of these potential disease-modifying agents transitioning from experimental to human osteoarthritis. Osteochondral explant models are highly valuable for determining joint-specific tissue responses.

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Beyond histology for assessment of joint degeneration: Proof-of-concept for contrast-enhanced micro-computed tomography in lumbar facet joints

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Introduction: Histology remains the gold standard in morphometric and pathological analyses of osteochondral tissues in human and experimental bone and joint disease. However, histological tissue processing is laborious, destructive and only provides a two-dimensional image in a single anatomical plane. Micro computed tomography (µCT) enables non-destructive three-dimensional visualization and morphometry of mineralized tissues and, with the aid of contrast agents, soft tissues. In this study, we evaluated phosphotungstic acid-enhanced (PTA) µCT to visualize pathology in human facet joint degeneration
Methods: Lumbar facet joint specimens were acquired from eleven patients undergoing decompression surgery. Fresh osteochondral specimens were immediately fixed in formalin and scanned in a benchtop µCT scanner (65 kV, 153 mA, 25 µm resolution). Subsequently, samples were completely decalcified in 5% formic acid, equilibrated in 70% ethanol and stained up to ten days in 1% PTA, which selectively binds to collagen. PTA-stained specimens were scanned at 70 kV, 140 mA, 15 µm resolution. Finally, specimens were destained and processed for routine tissue histology (HE staining).
Results: While conventional µCT only displayed mineralized bone tissue, PTA stained tissue samples showed X-ray attenuation in collagenous tissues including cartilage (collagen II, X), bone (collagen I) and bone marrow (collagen I, III, IV). Measurements of bone volume ($r = 0.90$, $p = 0.01$) and bone surface ($r = 0.95$, $p = 0.004$) were strongly correlated between conventional and contrast-enhanced CT methods. Image analyses of cartilage tissues enabled quantification of collagen loss in loaded versus unloaded regions of degenerated joints and visualization and quantification of cartilage cell (chondrocytes) numbers. Bone marrow signals corresponded with fibrovascular inflammatory cell infiltration in routine histology. Contrast-enhanced CT enabled quantification of inflammatory cell volume in bone marrow spaces.
Conclusions: PTA-enhanced µCT is a low-cost, non-toxic and highly feasible method for ex vivo 3D-visualization of osteochondral pathology in human joint tissues. The method enables bone morphometric analysis, as well as collagen distribution in all anatomical planes. Contrast enhanced µCT has several applications in bone and osteoarthritis research including 3D histopathological grading, tissue stratification, and imaging and analysis of aberrant collagen metabolism in osteochondral disease.

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Raumforderungen in der infrapatellaaeren Region

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Raumforderungen in der infrapatellaaeren Region haben eine breite Differenzialdiagnose. Das Wichtigste in der sonomorphologischen Differenzierung ist die praaezise anatomische Lokalisation im klinischen Kontext. Bei Raumforderungen in der infrapatellaaeren Region posterior des Ligamentum patellae sollte u.a. an diese Differenzialdiagnosen gedacht werden: Bursitis infrapatellaris profunda, Synovitis femorotibial mit allen mooeglichen Ursachen, Synovitis im Rezessus infrahoffaticus, Ganglien (mit Ursprung z.B. am vorderen Kreuzband oder Meniskus), benigne oder maligne ossaaere/kartilaginaaere Raumforderungen oder z.B. eine Laesion des Hoffa-Fettkoerpers (z.B. postoperativ). Beim Nachweis von Ganglien am Knie (und dies gilt ueberall am Bewegungsapparat) sollten immer Laaesionen von faserknorpeligen Strukturen (z.B. Meniskus), Ligamenten (z.B. vorderes Kreuzband) oder Sehnen gesucht, bzw. ausgeschlossen werden. Der Begriff «Hoffitis» sollte im modernen Ultraschallzeitalter nicht mehr benutzt werden, da es diese Entitaaet isoliert nicht gibt, d.h. in der Regel eine andere Pathologie zusaetzlich vorliegt, wie z.B. unter anderem eine Enthesitis, eine Synovitis oder ein Zustand nach Operation in der infrapatellaaeren Region mit inflammatorischer Mitbeteiligung des Hoffa-Fettkoerpers.

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Modulation of neutrophil extracellular traps using apremilast (PDE4 inhibition)

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Increased propensity for neutrophil extracellular trap generation has been described in autoimmune diseases such as rheumatoid arthritis. Neutrophil extracellular traps are thought to contribute to disease propensity. Calcium signalling is known to be important for neutrophil extracellular trap generation. Thus, controlling this calcium signalling pathway may allow for regulation of autoimmune disease pathology. Apremilast is a selective phosphodiesterase 4 inhibitor that is currently approved for the treatment of psoriasis and psoriatic arthritis with a positive phase 3 on Behcet`s disease. Inhibition of phosphodiesterase 4 can elevate cAMP levels, decrease adenylate cyclase levels and thus modulate calcium release and store-operated calcium signalling. We hypothesised that by inhibiting phosphodiesterase 4 with apremilast, calcium release can be controlled and in turn decrease the propensity for neutrophil extracellular trap generation. Reduction in PMA induced ROS production for healthy control neutrophils when treated with apremilast was observed. A decrease in PMA and calcium ionophore-induced neutrophil extracellular trap generation was also observed. Apremilast treatment of rheumatoid neutrophils also displayed a decrease in spontaneous ROS generation and neutrophil extracellular trap generation. We also investigated the effect of phosphodiesterase 7 inhibition. Interestingly, this displayed an opposite effect to phosphodiesterase 4 inhibition. By reducing neutrophil extracellular traps through modulation of calcium signalling by phosphodiesterase 4 inhibition, the possibility of controlling neutrophil extracellular trap generation in certain autoimmune conditions might be possible.

HPR – HEALTH PROFESSIONALS IN RHEUMATOLOGY IN SWITZERLAND

HPR 1

Entwicklung von Intake-Kriterien für ein Case-Management bei PatientInnen mit hoher Verweildauer auf der Klinik für Rheumatologie

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Ausgangslage: Auf die Klinik für Rheumatologie USZ werden immer wieder PatientInnen mit akuten, unklaren Schmerzzuständen eingewiesen. Für sie bedeutet diese Krise einer chronischen Erkrankung tagelanges Warten ohne gezielte Linderung. Grund dafür stellen u.a. Spezialuntersuchungen, Konsilien und Schmerzeinstellungen dar, die schwierig zu koordinieren sind. Dadurch entsteht ein erheblicher Zeitverlust, der sich auch betriebswirtschaftlich abbildet. 2018 überschritten 45 dieser PatientInnen (Swiss DRG I 68 C & E) die Zielverweildauer und verursachten ein erhebliches Defizit. Die Klinikleitung beschloss aus diesem Grund die Evaluation eines Case Managements (CM).
Ziele:
Frühzeitiges Erkennen der entsprechenden PatientInnen
Frühe Prozesskoordination
Reduktion der Leidens- Wartezeiten
Rasche Symptomkontrolle und Selbstversorgung
Reduktion der Verweildauerüberschreitung
Methode: Da ein CM aufwändig und nicht immer effektiv ist, müssen die richtigen PatientInnen ins CM aufgenommen werden. Dazu werden auf das Setting zugeschnittene Intake-Kriterien benötigt, die den gezielten Zugang ins CM steuern. Die medizinische Diagnose ist ein Kriterium, das 2018 aber nur bei 60% zu Verweildauerüberschreitungen führte. Weitere Kriterien (Psychiatrische Nebendiagnosen & psychosoziale Auffälligkeiten, komplexe Schmerzeinstellung, Opiat-Entzug, mehrere geplante med.-techn. Abklärungen & Konsilien, unklare OP-Indikationen) wurden entwickelt. Anhand dieser Kriterien wurden zwei Monate PatientInnen erfasst. Nach deren Austritt wurde überprüft, ob sie die Zielverweildauer überschritten und ob sich die Kriterien für ein CM-Intake eignen.
Ergebnisse: Im genannten Zeitraum wurden insgesamt 14 entsprechende PatientInnen erfasst. Davon überschritten 12 die Zielverweildauer durchschnittlich 5.3 Tage. Lediglich zwei Betroffene überschritten die Zielverweildauer nicht.
Schlussfolgerungen: Die Kriterien liefern verlässliche Parameter für den Einschluss in ein geplantes CM. Nun müssen Art und Umfang des CM überlegt werden. Faktoren wie geringe Fallzahlen, ungeplante Eintritte, massive Schmerzen, unklare Diagnosen, aufwändige Abklärungen und Assessments sind zu beachten. Die Komplexität erfordert ein erweitertes medizinisch-pflegerisches Fachwissen, Flexibilität, Leadership-Qualitäten, regelmässige Präsenz in der klinischen Praxis und eine gute Vernetzung. Dies lässt sich am besten mit der Tätigkeit einer Pflegeexpertin ANP integrieren.

HPR 2

Diagnostic test accuracy of clinical tests and ultrasound for the detection of cam and pincer morphology – a systematic review

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Background: Femoroacetabular Impingement (FAI) syndrome is seen as a predisposing factor for degenerative processes in the hip joint. Recognition and adequate intervention is needed to reduce the risk of premature degeneration. Several clinical tests for the diagnosis of FAI morphologies are proposed, but there is a lack of an actual systematic overview of the literature about the accuracy of these tests.
Objectives: To examine the diagnostic accuracy of clinical tests and ultrasound for the detection of pincer, cam or mixed type morphologies in people suspected of having FAI syndrome, and discusse the clinical utility of these tests.
Methods: A systematic search in PubMed, CINAHL, EMBASE and SPORTDiscus databases was conducted. Due to lack of data no meta-analysis was performed. Number of true and false positives, true and false negatives were extracted to calculate sensitivity, specificity, likelihood ratios and post-test probabilities. Several index tests were combined by multiplication of the corresponding likelihood ratios. Changes in post-test probabilities depending on varying disease prevalence were presented with the help of a plot showing the relationship between pretest and posttest probabilities.
Results: Nine studies were included, investigating 19 clinical tests plus ultrasound. Overall results showed a low specificity for all tests, ranging from 0.11 to 0.56. Sensitivity ranged from 0.18 to 1.00, with high sensitivities for FADIR, FPAW, maximal Squat test and ultrasound. A combination of these four tests with a negative test result showed a LR- of 0.12. Results are based on low quality evidence.
Conclusion: The current literature indicates that clinical tests are not appropriate to rule in a cam- or pincer-type morphology, but pain provocation tests and ultrasound can potentially be used to rule out a diagnosis of FAI syndrome with a negative test result.
Future projects planned: We would like to create a website for the presentation of a living systematic review on the diagnostic accuracy of clinical tests and ultrasound for the detection of pincer and cam morphology. For this, the results of the systematic review will be regularly updated after each newly published diagnostic test accuracy study. Additionally, we will include studies investigating asymptomatic people, hence without FAI syndrome but, being at risk of having cam or pincer morphology, such as ice hockey players, soccer players or dancers, and report these results separately.

HPR 3

A transition clinic or a clinic for young people – what's in a name? The challenges of developing a transition clinic from the ground up

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Introduction: Good transitional care with an individualised, structured but flexible management plan in a suitable phase of adolescence is essential to ensure a successful transition of care to adult services for young people with a chronic illness. Although caring for adolescents in evidence-based transition clinics improves patient outcomes, such clinics are not widely established in Switzerland. One of the main reason is the lack of funding for the necessary roles.
Aim: The aim of this project is to develop, implement and evaluate a transition clinic for patients with a chronic rheumatic disease.
Methodology: The methodology involved identifying a transition tool and stakeholders, defining a clinical pathway and measureable outcomes, involving users in this process and securing funding for the ANP role by Swiss health authorities.
Results: The clinic was initiated 01/2018. Patients were involved in naming the clinic. A successfully evaluated workshop was held with young people from the clinic in the first year. A structured clinic pathway was identified. No patients have been lost to follow up in this initial phase. Funding for the nurse role was secured for a second year as a result of these successes.
Discussion: Implementation of a transition clinic for patients with rheumatological diseases in Switzerland is challenging. We were able to start such a clinic due to private funding. Research projects aiming at measuring the effects of our structured transition clinic are planned and such research is needed to ensure funding. The goal is to be reimbursed through the hospital billing system.
Conclusion: The importance of empowering and supporting young people with a chronic illness to negotiate a successful transition from paediatric to adult services is widely recognised. In order to ensure the funding of such clinics, a structured clinic pathway with clear measurable outcomes is being established in Basel.
Acknowledgment: The Palatin Stiftung and the Gesellschaft für das Gute und Gemeinnützige Society (GGG) for their support of the project

HPR 4

A patient-centered approach for diagnosis and treatment of rheumatological diseases– a single center experience by an office based physician

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The complex diagnostic and therapeutic environment of chronic inflammatory diseases today challenges the modern physician in taking optimal decisions during all phases of disease management covering factors from patient satisfaction over practicability to cost effectiveness. In rheumatic diseases doctors still tend to focus on clinical parameters like tender and swollen joints. But even if these parameters improve, many patients experience insufficient subjective improvement to feel a notable difference to their quality of life. Inevitably, adherence decreases which - if unnoticed – leads to increased morbidity and mortality and is costly to manage.
Our center is designed to adapt to these conditions and offer our patients an approach that ensures patient satisfaction, adherence, practicability and thus therapeutic as well as economic outcome. With the intend of sharing best practice, this single center report describes a patient-centered approach and assesses patient satisfaction respectively.
In our model the interdisciplinary setting is assured by several cross-functional collaborations. Medical care through the physician is supported by easy accessible inhouse diagnostic procedures. Allied health professionals like physio- and ergotherapists cover preservation and rehabilitation of physical skills. The on-time drug delivery for treatment initiation, treatment application and patient support throughout therapy are conducted by the specialty pharmacy MediService and their specialized nurses. For covering emotional and mental care of the patient, we offer spiritual and pastoral support. Another unique point of differentiation is our individual educational support for patients in special life circumstances, e.g. nursing advice for female patients and their newborns.
Since March 2019 we assess patient satisfaction with a questionnaire on patient's contentment. A four-scaled rating was evaluated on several parameters concerning the quality of care. Preliminary analysis revealed an average rating of 3.9 of 4 points for the question on how well patients feel taken care of. Hosting and support together were rated with 3.4 as well as the provision with information on disease and treatment. Therefore, our clinic model not only suggests a practicable and proven combination of factors assuring patient satisfaction, adherence and therapeutic outcome but also contributes to health economy by an optimal care for rheumatology patients.

HPR 5

Dem Leiden eine Stimme geben

Die Erfassung des Leidensdrucks mittels Pictorial Representation of Illness and Self-Measure (PRISM) auf der Klinik für Rheumatologie im Universitätsspital Zürich

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1.Ausgangslage: PatientInnen auf der Klinik für Rheumatologie USZ, die für eine Komplextherapie eintreten, haben oft lange Krankheitsgeschichten. Im Anamnesegespräch fällt es ihnen schwer, ihr aktuelles Leiden präzise zu beschreiben. Die individuellen Auswirkungen ihrer Beschwerden und die Bedeutungszuschreibung ihrer Symptome finden dabei zu wenig Beachtung und kommen häufig erst später in informellen Gesprächen zutage. Die PatientInnen verlieren sich in ihren Erzählungen und können selten konkrete Bewältigungsstrategien benennen. Auch variieren ihre Geschichten häufig und erschweren einen interprofessionellen, ressourcenorientierten Behandlungsverlauf. Um den Leidensdruck und die Lebensqualität der Patienten erfassen zu können, wurde ein dafür geeignetes Instrument gesucht.
2.Ziele: Leiden der PatientInnen sind für sie selbst und im Behandlungsteam sichtbar und interpretierbar. Anamnesegespräche sind strukturiert einheitlich erfasst und dokumentiert. Bewältigungsstrategien werden erkannt, neue Strategien können entwickelt werden.
3.Methode: Das Instrument PRISM (Pictorial Representation of Illness and Self-Measure) wird durch Pflege in das Anamnesegespräch integriert. Es erfasst den Leidensdruck der PatientInnen und deren Bewältigungsstrategien. Die Ergotherapie fokussiert mit dem PRISM auf das Erarbeiten persönlicher Ressourcen und steuert den weiteren Betreuungsverlauf. PRISM ist das konzeptionell kohärenteste Instrument zur Erfassung von Leiden, ist verständlich, leicht anwendbar und liefert rasch persönliche Informationen. Es wird erfolgreich in anderen Settings eingesetzt. Eine A4-Tafel stellt «das Leben», ein fixer gelber Kreis in der rechten unteren Ecke das «Ich» dar. PatientInnen werden ermuntert, ihre «Krankheit» mit einem roten Magneten auf der Tafel in Bezug zum «Ich» zu setzen. Die Distanz zwischen dem «Ich» und dem «Krankheitsmagneten» wird PRISM-Distanz genannt und weist auf die Grösse des individuellen Leidensdrucks hin.
4.Ergebnisse und Ausblick: Die Nutzung von PRISM durch die Pflege hat sich bewährt. Leiden und Bewältigungsstrategien werden strukturierter und effizienter dokumentiert. Die Zusammenarbeit zwischen Pflege und Ergotherapie hat sich verbessert. Aktuell wird PRISM von Pflege und Ergotherapie unterschiedlich verwendet und dokumentiert. Dies erschwert einen interprofessionellen Behandlungsverlauf. Deshalb wurde eine gemeinsame Dokumentationsstruktur entwickelt, getestet und Anfang 2020 evaluiert.

HPR 6

Betätigungsfokussierte Gruppenedukation bei Menschen mit chronischen Schmerzen

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Hintergrund: Weltweit steigt die Zahl der chronischen Schmerzen, die einer Behandlung bedürfen. Aktuelle Evidenz zeigt sich im multimodalen Rehabilitationsansatz, welcher unter anderem die Klientenedukation beinhaltet. Die Edukation ist ein wichtiger Auftrag der Ergotherapie bei Menschen mit chronischen Schmerzen.
Ziel: Ziel dieser Review ist es, betätigungsfokussierte und edukative Interventionen für Klienten mit muskuloskelettalen chronischen Schmerzen bereitzustellen, welche für das Verständnis von Schmerz und der Alltagsbewältigung wirksam sind und in der ergotherapeutischen Gruppentherapie angewendet werden können.
Methode: Die Fragestellung wurde mittels einer Literaturreview beantwortet. Mit den Schlüsselwörtern Ergotherapie, Edukation, Schmerzmanagement und chronische Schmerzen, wurde in den Datenbanken MEDLINE, PubMed, CINAHL, PsycINFO, ERIC, AMED, IBSS und OTseeker nach Literatur gesucht. Die Studien wurden anhand von inhaltlichen und qualitativen Kriterien überprüft und in die Review ein- oder ausgeschlossen.
Ergebnisse: Die elf inkludierten Studien untersuchen vier Edukationsansätze zu unterschiedlichen Themenbereichen. Die Edukation zur neurophysiologischen Entstehung von Schmerz, Schulung zu Selbstmanagement und Coping, erfahrungsbasierte und betätigungsfokussierte Edukation und Rückenschulung zeigten einen positiven Effekt auf das Verständnis von Schmerzen der Klientinnen und Klienten und deren Alltagsbewältigung.
Schlussfolgerung: In Zusammenschau aller Ergebnisse zeigte sich, dass Edukation bei Menschen mit chronischen Schmerzen wirksam in Bezug auf verbesserte Ausführung von Betätigung und Schmerzintensität ist. Es gibt unterschiedliche evidenzbasierte Edukationsansätze, welche für die Umsetzung im ergotherapeutischen Gruppensetting geeignet sind und unterschiedliche Betätigungsbezüge aufweisen.

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