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FM 1

Tocilizumab for induction and maintenance of remission in giant cell arteritis – first randomized placebo-controlled trial

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Background: Tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor, showed rapid induction and maintenance of remission in published case series. This first RCT was intended to prove a beneficial effect.
Methods: This single-center, randomized, placebo-controlled trial included patients satisfying the 1990 American College of Rheumatology criteria for giant cell arteritis. Patients with new-onset or relapsing disease were randomized in a 2:1 ratio to receive either tocilizumab (8 mg/kg) or placebo intravenously. Thirteen infusions were given in 4-week intervals. Both arms received oral prednisolone, starting at 1 mg/kg/d and tapered down to 0 mg according to a standard protocol. The primary outcome was defined as the number of patients with complete remission at a prednisolone dose of 0.1 mg/kg/d (week 12).
Results: Seventeen out of 20 tocilizumab-treated and 4 out of 10 placebo-treated patients reached complete remission by week 12 ($p = 0.03$). Relapse-free survival was achieved in 17 tocilizumab-treated and 2 placebo-treated patients by week 52 ($p = 0.008$). The mean survival-time difference to stop glucocorticoids was 12 weeks in favor of tocilizumab ($p < 0.001$), leading to a cumulative prednisolone dose of 43 mg/kg in the tocilizumab group versus 110 mg/kg in the placebo group ($p < 0.001$) after 52 weeks. Seven patients in the tocilizumab group and 5 in the placebo group experienced serious adverse events.
Conclusion: This first randomized controlled trial demonstrates the efficacy of tocilizumab in the induction and maintenance of remission in patients with giant cell arteritis.

FM 2

Incidences and Predictors of Organ Manifestations in the Early Course of Systemic Sclerosis: A Longitudinal EUSTAR Study

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Background: Systemic sclerosis (SSc) is a rare and clinically heterogeneous autoimmune disorder characterised by fibrosis and microvascular obliteration of the skin and internal organs, particularly the heart, lungs, kidneys and the digestive tract. Organ involvement mostly manifests after a variable period of the onset of Raynaud's phenomenon (RP). Using data from the large, multinational EUSTAR cohort, we aimed to map the incidence and predictors of pulmonary, cardiac, gastrointestinal (GI) and renal involvement in the early course of SSc.
Methods: Patients from the EUSTAR cohort with early SSc, defined as those who had a visit within the first year of RP onset were studied. Outcome measures were analysed as a function of time after RP onset using Kaplan-Meier methods, and Cox regression analysis was used to evaluate predictors of incident organ manifestations.
Results: Out of the 9,891 patients in the EUSTAR database who fulfilled the ACR criteria for SSc, 695 patients had a baseline visit within one year after RP onset. The incident non-RP manifestations (in order of frequency) were: skin sclerosis (75%) GI symptoms (71%), impaired diffusing capacity for monoxide <80% predicted (65%), digital ulcers (34%), cardiac involvement (32%), impaired forced vital capacity (FVC) of <80% predicted (31%), increased resting systolic pulmonary artery pressure estimated by echocardiography (PAPsys)>40mmHg (14%), and renal crisis (3%). In the heart, incidence rates were highest for diastolic dysfunction followed by conduction blocks and pericardial effusion. While the main baseline risk factor for a short timespan to develop FVC impairment was diffuse skin involvement, for PAPsys >40 mmHg it was higher patient age. The main risk factors for incident cardiac manifestations were anti-topoisomerase autoantibody positivity and older age. Male sex, anti-RNA-polymerase-III positivity, and older age were risk factors associated with incident renal crisis.
Conclusion: In this study of incidence rates in SSc patients presenting early after RP onset, approximately half of all incident organ manifestations occur within two years and have a simultaneous rather than a sequential onset. These findings have implications for the design of new diagnostic and therapeutic strategies aimed to 'widen' the still very narrow 'window of opportunity'. They may also enable physicians to counsel and manage patients presenting early in the course of SSc more accurately.

FM 3

Rebound-associated vertebral fractures after denosumab discontinuation: A series of 9 women with 50 spontaneous vertebral fractures.

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Osteoporosis (OP) treatments are given for a limited period of time because of a risk / benefice balance. Reversibility of OP treatment is observed by the measurements of bone markers turnover (BMTs) and bone mineral density (BMD). The effect on vertebral fracture (VFx) is difficult to evaluate. The OP treatment discontinuation is associated with an increase of BMTs and a more or less rapid decrease of BMD. Denosumab (Dmab) discontinuation is associated with a severe rebound effect on BTMs and BMD for near 24 months. A recent publication suggests an increase of VFx (Osteoporos Int. 2015 Oct 28). We report the cases of 9 postmenopausal women. They received Dmab 60mg every 6 months for 2 to 8 doses. The 9 women were on calcium and vitamin D. A wide biological assessment excluded a secondary cause of OP. VFx were documented by MRI.
Five OP women without any prior fragility fracture were treated every 6 months with 4 to 6 Dmab doses. Dmab was stopped because there was no more OP on BMD (3 women 55, 56 and 59 y old), the aromatase inhibitors were stopped (77y old) and according to the wish of the patient (77y old). 9 to 16 months after Dmab discontinuation, they presented respectively 5 (D11, D12, L2-L4), 9 (D7-D9, D12-L5), 2 (D11 and D12), 5 (D12-L2) and 9 (D5-D9 and D11-L2) symptomatic spontaneous (SS) VFx.
A 65 y old woman with osteoporosis and 1 prevalent VFx was treated every 6 months with 8 Dmab doses. Ten months after Dmab discontinuation she presented 6 SSVFx (D5, D8, D12, L2-L4).
These 62 y old woman (osteopenia, treated with aromatase inhibitors) received 2 Dmab doses every 6 months. The subsequent Dmab dose was forgotten. Twelve months after the last Dmab dose she presented a D10 SSFx.
A 71 y old woman (one prevalent VFx and one hip fracture) received 2 Dmab doses with a delay of 11 months because of a lack of compliance. Eleven months after the last Dmab dose she presented 5 SSVFx (D12, L2-L5).
Conclusion: These 9 cases show a severe increased risk of vertebral fractures in the 9 to 16 months after the last injection of Dmab. The occurrence of these fractures can be explained by the severe rebound effect observed after denosumab discontinuation. It is urgent to: 1) inform the health authorities and patients of this risk; 2) determine treatment regimens before or at the time of denosumab discontinuation.

P 1

Efficacy and safety of baricitinib in patients with rheumatoid arthritis and inappropriate response to conventional disease-modifying anti-rheumatic drugs: 24-week phase 3 RA-BUILD study summary results

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Background: We present efficacy, safety and patient-reported outcome (PRO) analyses from patients with active rheumatoid arthritis (RA) and inappropriate response (IR) to csDMARDs in the randomised 24-week (wk) phase 3 RA-BUILD study of baricitinib, an oral JAK1/2 inhibitor.
Methods: Patients with active RA and IR to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs; N = 684) received placebo or baricitinib (2 or 4 mg,QD) for 24 weeks. Primary endpoint was ACR20 response at wk12 for baricitinib 4 mg vs placebo. Safety and other efficacy analyses were also reported.
Results: Significant improvements in ACR 20/50/70, DAS28-ESR, SDAI remission, HAQ-DI, and faster decreases in morning joint stiffness, worst joint pain and tiredness were seen with baricitinib vs placebo at wk12 and wk24. At wk24, mTSS was reduced with baricitinib 4 mg vs placebo. Baricitinib 4mg produced a significant rapid decrease (within 1wk) in DAS28-ESR and CDAI vs placebo. TEAE and SAE rates, including serious infections, were similar among groups. Increases in total lymphocyte count (TLC) including T, B and NK cells at wk4 for baricitinib were within the normal ranges. T-cells and NK-cells decreased and B-cells increased at wk12 and wk24 vs placebo.
Conclusions: Baricitinib 4mg resulted in significant improvement in structural progression and PROs at wk12 and wk24. Safety and infection rates were acceptable regardless of TLC changes.

P 2

Baricitinib, methotrexate, or baricitinib plus methotrexate in patients with early rheumatoid arthritis who had received limited/no treatment with disease-modifying anti-rheumatic drugs: Phase 3 trial results

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Background: We report results from a phase 3 study of baricitinib.
Methods: Patients with active RA (TJC&SJC ≥6, hsCRP ≥3.6 mg/L) and no previous disease-modifying anti-rheumatic drugs (DMARDs) other than ≤3 doses of methotrexate (MTX) were randomized to MTX, baricitinib 4 mg QD, or baricitinib 4mg QD+MTX for ≤52wks. MTX (± baricitinib) was up-titrated from 10 to 20mg QW over 8wks. The primary objective evaluated non-inferiority of baricitinib monotherapy to MTX on ACR20 at Wk24.
Results: Of 584 randomized patients, 87%, 91%, and 89% completed Wk24 in the MTX, baricitinib, and baricitinib+MTX groups, respectively. ACR20 response at Wk24 was higher with baricitinib monotherapy vs MTX (77% vs 62%; p ≤.01). Baricitinib produced greater improvements in secondary disease activity measures than MTX as early as Wk1. Baricitinib+MTX did not appear to increase the benefit observed with baricitinib monotherapy. Clinical remission was seen in significantly higher proportions of patients receiving baricitinib or baricitinib+MTX vs MTX alone. TEAE and SAE rates were similar across groups. Through 24wks, 2 (1.0%), 6 (3.8%) and 14 (6.5%) patients discontinued because of an AE in the MTX, baricitinib, and baricitinib+MTX groups, respectively.
Conclusion: All groups experienced disease activity improvements; baricitinib monotherapy produced significantly larger, more rapid improvements and higher rates of remission compared to MTX monotherapy, with a satisfactory safety profile.

P 3

Efficacy and safety of baricitinib in patients with active rheumatoid arthritis and inadequate response to tumour necrosis factor inhibitors: 24-week phase 3 RA- BEACON study results

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Background: Baricitinib (BARI), an oral JAK1/JAK2i, was investigated in the phase 3 RA-BEACON study.
Methods: 527 patients with active rheumatoid arthritis (RA) despite previously using ≥1 tumour necrosis factor inhibitor (TNFi) were randomised to placebo (PBO) or BARI (2 or 4 mg, QD). Primary endpoint was wk12 ACR20 (BARI 4 mg vs PBO). Subgroup efficacy by prior biologic use, safety, and changes in total lymphocyte count (TLC) and NK-cells are reported.
Results: Wk12 ACR20 was higher with BARI 4mg vs PBO (55% vs 27%;p ≤0.001). Improvements in ACR20/50/70,DAS28-CRP occurred with BARI 4 mg (1 prior TNFi) at wk12/wk24; improvements in CDAI;SDAI;HAQ-DI were observed at wk24. A decrease ≥0.6 in DAS28 and ≥6 in CDAI at wk4 was observed in 79% and 80% of patients on BARI 4mg, respectively, associated with LDA/remission at wk12/wk24. More TEAEs occurred with BARI 2 and 4mg vs PBO, including infections. TLC changes in BARI groups were similar vs PBO at wk12/wk24. There were increases in T-cells, B-cells and NK-cells at wk4, and decreases in T-cells, NK-cells, and an increase in B-cells at wk12/wk24 for BARI groups (all TLC changes within normal range; NK- cell decrease was not associated with increased infection).
Conclusions: BARI showed clinical improvements wk4–wk24 with acceptable safety profile. Wk4 clinical response might predict later LDA/remission.

P 4

Predictors for the development of anti-citrullinated protein antibodies in individuals genetically at risk for rheumatoid arthritis

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Background: Different risk factors may be relevant for the development of this systemic autoimmunity, one of the phases preceding the onset of rheumatoid arthritis (RA).
Objective: To identify predictors for the development of systemic autoimmunity associated with RA in individuals genetically at increased risk.
Methods: This is an ongoing prospective cohort study of individuals at increased risk of developing RA, namely first degree relatives of patients with RA (FDRs). Those without clinical evidence of RA were enrolled and followed-up yearly. We included all subjects with available anti-citrullinated protein antibodies (ACPA) status (anti-CCP 2, 3.0, or 3.1). We used logistic regression to analyze univariable and multivariable associations between ACPA positivity and putative risk factors or symptoms, including the Connective Tissue Disease Screening Questionnaire (CSQ), 3 or more positive responses represented possible RA.
Results: A total of 1064 of FDRs were analyzed, of which 57(5%) were ACPA- positive. FDRs had a median age of 45 (interquartile range(IQR): 34–56) years, 76% were female, 25% had at least one self-reported episode of joint swelling, however on examination only 12% had >1 swollen joint. In univariable analyses, ACPA-positivity was associated with older age, female sex, tender joints (self reported, on examination and mean count), mean swollen joint count, CSQ score and self-reported symptoms associated with possible RA by CSQ. Tobacco smoking, alcohol consumption, obesity or tooth loss were not

significantly associated with ACPA status. In women, ACPA-positivity was significantly associated with age (OR: 1.1, 95%CI: 1.0–1.1), but not in men (OR:1.0, 95%CI:0.9–1.1). In the multivariable adjusted analysis, older age than 46 (OR: 3.2, 95%CI:1.2–8.0) and self reported symptoms associated with possible RA (OR: 2.4, 95%CI:1.1–5.2), remained independently associated with ACPA positivity. Female sex and tobacco smoking ever had a strong but not significant association.
Conclusions: In individuals at high risk for RA, the development of ACPAs was associated with older age and self reported symptoms related with possible RA.We found a trend for an association between female sex and tobacco smoking with ACPA positivity, which did however not reach statistical significance. These findings suggest similar risk factors for the development of ACPAs and for classifiable RA, suggesting that the development of ACPAs is a valid proxy for RA development.

P 5

Immediate Release of Peripheral Neutrophil Myeloperoxidase and Elastase and Formation of Extracellular Traps up to Cigarette Smoking in Rheumatoid Arthritis

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Background: Smoking is an independent risk factor for rheumatoid arthritis (RA) [1]. In response to infectious agents, neutrophil granulocytes extrude their nuclear contents known as neutrophil extracellular traps (NETs) [2]. RA neutrophils display a vastly greater NET formation than normal neutrophils [3, 4]. Since NETs are proinflammatory and immunostimulatory and neutrophils show increased activity in inflammatory lung conditions, we investigated the responsiveness of peripheral blood neutrophils in RA to cigarette smoke.
Methods: Regular smokers with RA (n = 6) and without (n = 9) were examined at baseline and after a 16 hour abstinence from smoking. After smoking of 2 cigarettes within 10 min measurements were repeated at 0, 30, 60 and 120 min. Parameters included exhaled carbon monoxide (CO), myeloperoxidase (MPO), neutrophil elastase (NE) and cell free nucleosomes, measured by ELISA. Routine laboratory tests included blood counts, CRP, BSR and clotting parameters. In addition, neutrophils from healthy donors were incubated with cigarette smoke extract (CSE) for assessing NET formation by SytoxGreen extracellular DNA staining and combined immunohistochemistry (ICH) with anti-MPO, anti-cit-H3 and DAPI.
Results: RA smokers and controls showed similar courses of CO levels. RA neutrophils displayed higher baseline levels for MPO, NE and nucleosomes. In RA patients, re-exposure to smoke caused a pronounced increase of leucocytes and neutrophils, a 3- fold rise of MPO und NE at 30 minutes after re-exposure and a subsequent time-dependent reduction up to 120 min. Unexpectedly, this was paralleled by a sharp reduction in circulatory cell free nucleosomes. No changes were observed concerning parameters of inflammation and clotting. *In-vitro,* freshly isolated control neutrophils also showed diminished PMA-driven NET release after treatment with CSE.
Conclusions: In RA, peripheral blood neutrophils are pre-activated. Moreover, cigarette smoking provokes immediate release of toxic neutrophil granular enzymes into the circulation and transient reduction of NET formation, reflecting the systemic effect of smoking. The reduced NET formation *in-vivo* was unexpected, but was confirmed by the diminished CSE-induced NET formation *in-vitro.*

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P 6

Functional disability and its predictors in systemic sclerosis: a study from the DeSScipher project within the EUSTAR group

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Background: Systemic sclerosis (SSc) can greatly impact the patients' quality of life due to the multisystem manifestations. The health assessment questionnaire (HAQ) is one of the most commonly used measures of disability in musculoskeletal disorders and was extended to form the scleroderma HAQ (SHAQ), a more disease-specific disability scale that incorporates the HAQ and 5 visual analogue scales (VAS) into one score. This study aims to identify contributors of disability in SSc by means of the SHAQ.
Methods: Adult patients from the DeSScipher cohort were included in the analysis if they had one complete SHAQ (range 0–3) recorded and fulfilled either the 1980 ACR or the 2013 ACR/EULAR criteria for SSc. Multiple linear regression analysis was used to assess the combined effect of factors possibly associated with disability. Variables included in the model were defined a priori.
Results: 813 patients had one complete SHAQ recorded between June 2013 and January 2016 (34% of all patients followed in the DeSScipher cohort).
The patients had a mean SHAQ score of 0.86 (standard deviation [SD] 0.65) and an average HAQ score of 0.92 (SD 0.77). 60% of patients were in the "mild to moderate difficulty" SHAQ category (score of 0–1), 34% in the "moderate to severe disability" category (score of 1–2) and 6% in the "severe to very severe disability" category (score of 2–3). In order of magnitude, the means of the five VASs included in the SHAQ were: overall disease severity (36 mm, SD 26), Raynaud's phenomenon (30 mm, SD 28), pulmonary symptoms (23 mm, SD27), gastrointestinal symptoms (19 mm, SD 25) and digital ulcers (19 mm, SD 18).
In multiple linear regression, the main contributor to functional disability was dyspnoea. The SHAQ scores reported by patients with NYHA class 4, 3 or 2 were on average 0.65 units (95% confidence interval [CI] 0.30–1.01), 0.58 units (95%CI 0.41–0.75) and 0.19 units (95%CI 0.10–0.27) higher than that of patients with NYHA class 1. The presence of fibromyalgia (0.41 units, 95%CI 0.21–0.62) as well as muscle weakness (0.25 units, 95%CI 0.14–0.36) were also associated with higher levels of disability. Patients reporting oesophageal, gastric and intestinal symptoms simultaneously had, on average, a SHAQ score of 0.45 units (95% CI 0.33–0.58) higher than patients reporting no gastrointestinal symptoms.
Conclusions: Patients perceive dyspnoea, pain, muscle weakness and gastrointestinal symptoms as the main factors driving their level of disability.

P 7

Nodular regenerative hyperplasia of the liver – a rare vascular complication of systemic sclerosis

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Background: Nodular regenerative hyperplasia (NRH) is a rare liver disease causing non-cirrhotic intrahepatic portal hypertension with life-threatening complications. Among the autoimmune diseases, SSc has been hypothesized to be associated with NRH. Since in both entities microvascular injury is considered one of the earliest pathologic events, it might be hypothesized that NRH represents a yet unidentified vascular complication of SSc.
Objectives: To investigate the prevalence and clinical phenotype of NRH in SSc.
Methods: Published cases of SSc-NRH were identified by systematic literature review. Next, we screened the Zurich SSc cohort. In accordance with international guidelines, the diagnosis of NRH had to be established by liver biopsy showing a characteristic diffuse micronodular transformation without fibrous septa. SSc characteristics were derived from the EUSTAR database. Information on NRH was extracted from the patients' charts. The study was approved by the local institutional review board.
Results: The Pubmed search review retrieved 9 cases of SSc-NRH. In the Zurich cohort, 5 out of 278 patients with established SSc were diagnosed with NRH resulting in a prevalence of 1.8%. The majority of patients was female (69.2%). Mean age was 44.5 ± 12.3 years at diagnosis of SSc with a disease duration of 8.2 ± 7 years when NRH was diagnosed. NRH occurred in diffuse and limited cutaneous SSc. In most patients, vascular features of SSc were present at the diagnosis of NRH including digital ulcers (ever 100%, active 71.4%), an active pattern on nailfold capillaroscopy (100%), and pulmonary hypertension (50%). The most prevalent auto-antibodies were anti-centromere (40%) and anti-U1nRNP (33%), whereas no patient was positive for anti-Scl70 or anti-RNA- Polymerase III. In most patients, an elevation of AP and GGT (75%, 60%) occured, whereas transaminases were not increased. Melaena and hematemesis occurred in 66.7%, resp. 50% of patients. Ultrasound detected ascites (60%) and splenomegaly (75%), but no pathologic liver morphology, although an increased stiffness was diagnosed by fibroscan (75%). Portal hypertension was diagnosed in 85.7% with oesophageal varices (70%) and variceal haemorrhage (44.4%) as main complications.
Conclusion: NRH might represent a rare, yet clinically important, potentially life-threatening complication in SSc patients, especially in those with prominent vascular features and positivity for anti-centromere.

P 8

Impaired micronutrient status in patients with systemic sclerosis

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Background: Micronutrients are essential dietary factors involved in many metabolic processes like oxidative stress, collagen synthesis and wound healing, which are also important for the pathogenesis of systemic sclerosis (SSc). Given the frequent gastrointestinal involvement and impaired nutritional status, we hypothesized that micronutrients could be profoundly affected in SSc patients.
Methods: Patients meeting the ACR/EULAR 2013 classification criteria for SSc were prospectively recruited between 2009–2014. Clinical assessment, data recording and quality controls were done according to EUSTAR standards. In addition, the UCLA SCTC-GIT 2.0 questionnaire was applied and the circulating levels of several micronutrients were measured: zinc, selenium, prealbumin, holotranscobalamin, vitamin B12, folic acid, red cell folate. Patients with micronutrient deficiency (-ies) were compared to those with a normal micronutrient pattern. The two-sided Fisher's exact test, double T-test and the Mann-Whitney U-test were used, as appropriate. Binary logistic regression was applied to identify risk factors for deficiency in micronutrients.
Results: Nearly half (44%) of the 176 patients with SSc included into the study showed a deficiency in at least one of the measured micronutrients, most frequently in selenium (22%), folic acid (17%) and prealbumin (15%). Nearly a fifth (19%) of these patients had multiple deficiencies. There was a significant association between low levels of zinc and selenium, prealbumin and folic acid, respectively. Patients with lower body mass index had significantly lower zinc levels, and those with low prealbumin had more frequent stomach symptoms. Advanced skin fibrosis (higher modified Rodnan skin score, p = 0.007; skin thickening proximal to the metacarpophalangeal (MCP) joints, p = 0.009; positive ACR 1980 classification criteria, p = 0.014), as well as lower hemoglobin levels (p <0.001), were strongly associated with deficiency in micronutrients. The predictive model revealed skin thickening proximal to MCP as strongest risk factor for deficiency in micronutrients (OR 4.96, 95%CI [1.1–22.4], p = 0.037).
Conclusion: Deficiencies in micronutrients are a frequent and often complex burden in patients with SSc. Especially patients with more advanced skin fibrosis are at high risk for an impaired micronutrient status. These novel data have potential clinical implications, suggesting that screening for micronutrients should be performed in these patients.

P 9

Early detection of lung involvement in systemic sclerosis using molecular targeted nuclear imaging

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Background: Interstitial lung disease (ILD) is one of the major causes of systemic sclerosis (SSc)-related deaths. Since routine diagnostics including high resolution CT and pulmonary function tests only detect irreversible organ damage, there is an urgent need for the non-invasive diagnosis of ILD at earliest, still reversible disease stages.
Objective: Therefore, we assessed nuclear imaging as a highly sensitive methodology for the early detection of SSc-ILD by targeting integrin $\alpha_v\beta_3$ as a pathophysiologic key molecule of early inflammation-dependent fibrosis.
Methods: Expression of integrin $\alpha_v\beta_3$ was analysed in lung sections from patients with SSc-ILD, idiopathic pulmonary fibrosis (IPF), healthy controls as well as from bleomycin- challenged mice and Fra-2 transgenic (tg) mice using immunohistochemistry. *In vivo* small animal SPECT (single photon emission computed tomography) imaging was performed at early disease time points to visualise inflammation-dependent pulmonary fibrosis using ^{177}Lu-DOTA-RGD radioconjugates specifically targeting integrin $\alpha_v\beta_3$. The specific pulmonary accumulation of the radiotracer was confirmed by *ex vivo* SPECT/CT scans, biodistribution, and autoradiography studies.
Results: Expression of integrin $\alpha_v\beta_3$ was significantly increased in lung sections of patients with SSc-ILD and IPF versus healthy controls (p <0.009, p <0.02). In line with the results observed in the human diseases, lungs of bleomycin-treated and Fra-2 tg mice showed higher expression levels of integrin $\alpha_v\beta_3$ as compared to controls (p <0.03 each). Notably, nuclear SPECT/CT with ^{177}Lu-DOTA-RGD targeting integrin $\alpha_v\beta_3$ successfully visualised pulmonary inflammation and incipient fibrosis in the model of bleomycin-induced lung fibrosis at day 7. Consistently, imaging of integrin $\alpha_v\beta_3$ in Fra-2 tg mice at 13 weeks of age, the starting point of pulmonary fibrosis, showed a higher pulmonary radiotracer accumulation compared with wild type littermates. *Ex vivo* SPECT/CT scans, biodistribution and autoradiography studies of isolated lungs confirmed the *in vivo* results and validated the specific tracer uptake in lungs from bleomycin-challenged mice and Fra-2 tg mice.
Conclusion: Our data provide evidence that targeting pathophysiologic key molecules of inflammation-dependent fibrosis with nuclear imaging is a promising sensitive, non- invasive approach for the early detection of lung involvement in SSc.

P 10

Safety and efficacy of extracorporeal shock wave therapy (ESWT) in calcinosis cutis associated with systemic sclerosis

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Objective: Calcinosis cutis is a frequent, difficult to treat manifestation of systemic sclerosis (SSc) associated with high morbidity. The aim of this prospective, controlled, monocenter study was to assess safety and efficacy of extracorporeal shock wave therapy (ESWT) for calcinosis cutis of the finger in SSc patients.

Methods: A 12 week proof of concept study in which 4 SSc patients with calcinosis cutis were treated at one painful finger with high-energy, focused ESWT, in 3 sessions with one week interval between each session. A second, untreated finger, served as control. The outcome parameters were change in pain, change in size of calcification measured by ultrasound (US) and computed tomography (CT) and of the force by pressing the finger against a Dolorimeter.
Results: Pain was reduced (by 91% and 60%) in the treated finger in two out of four patients. There was no change in the control fingers. The size of the calcinosis in the treated finger was reduced in three (US) and four patients (CT). Inter-assessor agreement was acceptable for US volume measures (ICC = 0.863)
Conclusion: We could show promising evidence for safety and efficacy of EWST for chronic, treatment resistant calcinosis cutis in SSc patients, thus justifying the initiation of larger multicenter controlled trials.

P 11

Occurence of anti-Infliximab antibodies and associated co-factors in children with refractory arthritis and/or uveitis

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Background: Infliximab (IFX) is a monoclonal TNF-alpha inhibiting antibody used for the treatment of children with refractory arthritis and/or uveitis. In adults, immunogenicity is associated with infusion reactions and lack of clinical response. In children, corresponding data are scarce. We aimed to describe the occurrence of anti- IFX antibodies and determine co-factors associated with anti-IFX antibodies.
Methods: A longitudinally observed cohort of consecutive (2009-2012) children treated with IFX was retrospectively analyzed. Blood samples were collected every 6 months before IFX infusion and tested for anti-IFX antibodies using Radio Immuno Assay. Clinical characteristics and potential co-factors were reviewed in the patients' records. Associations to the presence of anti-IFX antibodies were quantified by bivariate odds ratios (OR). Stepwise multivariate logistic regression included all significant bivariate co-factors providing adjusted ORs.
Results: Anti-IFX antibodies occurred in 14/62 treated children (23%) and in 32/253 tested blood samples (12.6%). Infusion reactions were observed in 10/62 (16%) children during the treatment period and were highly associated with anti-IFX antibodies (bivariate OR = 15.00 / multivariate OR = 11.32). Further statistically significant co-factors were: young age (means 7.01 versus 9.88 years) and absence of uveitis as indication for IFX treatment (bivariate OR = 6.00 / multivariate 9.09).
Conclusion: Anti-IFX antibodies occurred frequently and at any time during IFX treatment. The high associations of IFX antibodies with young age, infusion reactions, and arthritis without uveitis may have consequences for therapeutic management in future. However, prospective data of large, representative cohorts are needed.

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P 12

A Randomized, Double-blind, Active- and Placebo (PBO)-controlled Phase 3 Study of Efficacy and Safety of Ixekizumab (IXE), Adalimumab (ADA), and Placebo Therapy in Patients Naïve to Biologic Disease-modifying Antirheumatic Drugs (bDMARDs) with Active Psoriatic Arthritis (PsA)

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Introduction: IXE is an anti-IL-17A monoclonal antibody under investigation for PsA treatment.
Methods: 417 bDMARD-naïve patients with active PsA were randomized to PBO (N = 106), ADA 40 mg Q2W (N = 101), or IXE 80 mg Q2W (N = 103) or Q4W (N = 107) after an initial 160 mg dose. Endpoints included ACR20 response at 24 weeks (primary), ACR50/70, PASI75/90/100, DAS28-CRP, LDI-B, LEI, and HAQ-DI (12 and 24 weeks), and mTSS (16 and 24 weeks).
Results: 382 patients completed 24 weeks: 30.2%, 57.4%, 62.1% and 57.9% of PBO-, ADA-, IXE Q2W- and IXE Q4W patients, respectively, had ACR20 responses. At 12 (ACR70 not eligible for comparison) and 24 weeks, a higher percentage of IXE Q2W/IXE Q4W- than PBO patients achieved ACR20/50/70 and PASI75/90/100 responses ($p \leq .001$).IXE groups experienced greater reductions than PBO in LDI-B ($p \leq .025$) and LEI (Week 12 Q2W only; $p \leq .05$). DAS28-CRP and HAQ-DI scores improved, and both IXE doses inhibited radiographic progression of joint structural damage (mTSS) ($p \leq .025$ vs PBO). 24-week treatment-emergent adverse events (TEAE) incidence was higher ($p \leq .025$) with IXE and ADA vs PBO. Discontinuation due to TEAE was similar across groups. No deaths occurred.
Conclusion: IXE patients showed greater disease marker improvement than PBO and no unexpected safety findings were observed in bDMARD-naïve patients with PsA.

P 13

Safety and Tolerability of Secukinumab in Patients With Active Ankylosing Spondylitis: Pooled Safety Analysis of Two Phase 3, Randomized, Controlled Trials

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Background: Secukinumab, an anti–IL17A monoclonal antibody, improved signs and symptoms of ankylosing spondylitis (AS) in 2 randomized double-blind placebo (PBO)-controlled studies, MEASURE 1 and 2.1,2 Here, we report pooled safety data through ≥52wks from these studies.
Methods: In MEASURE 1, 371 patients (pts) with active AS fulfilling the modified New York Criteria were randomized to secukinumab or PBO. Pts on secukinumab received 10mg/kg intravenously (IV) at baseline, Wk2 and 4, followed by 75 or 150 mg subcutaneously (SC) every 4wks (q4w) from Wk8. PBO was given according to the same IV to SC schedule. In MEASURE 2, 219 pts were randomized to receive SC secukinumab (75/150 mg) or PBO at BL, Wk1, 2, and 3, and q4w starting from Wk4. At Wk16, PBO pts were re-randomized to receive secukinumab 75/150 mg SC q4w. Anti-drug antibodies (ADAs) were assessed using a Meso Scale Discovery bridging assay. Safety data were pooled at the pt level with a data cut-off of Wk52 visit of the last pt enrolled in each study.
Results: 571 pts received ≥1 dose of secukinumab (691.1pt-yrs of exposure). Demographic and disease characteristics were well-balanced in the secukinumab and PBO populations. The incidence of adverse events (AE)/serious AEs (SAE) during the 16wk PBO-controlled period was 65.7/3.3% and 58.7/4.1% in the secukinumab and PBO groups. Incidence rates of AE/SAEs across the entire safety period (mean exposure: secukinumab, 442.1days; PBO, 118.5days) were 206.8/7.9 and 359.5/12.8 per 100 pt-yrs with secukinumab and PBO; 27 (4.7%) pts receiving secukinumab and 11 (5.6%) for PBO discontinued due to AEs. Three deaths were reported: 1 suicide (PBO); 1 due to respiratory failure (IV→75 mg) and 1 due to an acute myocardial infarction (75 mg), both pts with multiple cardiovascular risk factors. During the entire study period nasopharyngitis was the most frequent AE with secukinumab (17.9 per 100 pt-years vs 19.5 in PBO). The incidence (per 100 pts-yrs) of inflammatory bowel disease (1.2) and *Candida* infections (0.9) with secukinumab was low. Uveitis AEs were reported in 7 (1.2%) pts on secukinumab and 2 (1.0%) on PBO and ADAs were detected in 2 (0.3%) pts (efficacy maintained). There were no suicidality-related AEs with secukinumab.
Conclusion: Secukinumab was well-tolerated in pts with active AS, with a low incidence of SAEs and discontinuations due to AEs.

[1]Baeten, et al. Arthritis Rheumatol. 2014;66(11Suppl):S360
[2]Sieper, et al. Arthritis Rheumatol. 2014;66(11Suppl):S232

P 14

Secukinumab Efficacy in Anti-TNF-Naive Patients and Patients Previously Exposed to Anti-TNF Therapy: Results of A Randomized, Double-Blind, Placebo- Controlled Phase 3 Study (MEASURE 2) in Active Ankylosing Spondylitis

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Background: Current treatment options for ankylosing spondylitis (AS) patients with intolerance or an inadequate response to tumor necrosis factor alpha inhibitors (anti-TNF) are limited. Secukinumab, a human anti–interleukin-17A monoclonal antibody, significantly improved the signs and symptoms of AS in the phase 3 MEASURE 2 study [1].
Objective: To evaluate the efficacy and safety of secukinumab by anti-TNF history in the MEASURE 2 study.
Methods: 219 adults with active AS were randomized to receive subcutaneous (s.c.) secukinumab (150 or 75 mg) or PBO at baseline, Wk 1, 2 and 3, and every 4 wks starting at Wk 4. Randomization was stratified according to prior anti-TNF experience: anti-TNF-naive, or inadequate response or intolerance to not more than one anti-TNF biologic agent (anti-TNF-IR). At Wk 16 PBO-treated subjects were re-randomized to secukinumab 150 or 75 mg. Pre-planned subgroup analyses of the primary and secondary endpoints were conducted among anti-TNF-naive and anti-TNF-IR subjects and included: the proportion of subjects achieving an Assessment of Spondyloarthritis International Society (ASAS) 20 response (primary endpoint), ASAS40, high sensitivity C-reactive protein (hsCRP), ASAS 5/6, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Short Form-36 (SF-36), Ankylosing Spondylitis Quality of Life (ASQoL), and ASAS partial remission. Analyses at Wk 16 used non-responder imputation (for binary variables) and mixed-effects repeated measures model (for continuous variables). Wk 52 data are as observed.
Results: 62% of subjects enrolled were anti-TNF-naive and 38% were anti-TNF-IR. At Wk 16, secukinumab 150 mg (but not 75 mg) improved ASAS20 response rates compared with PBO in both anti-TNF-naive (68.2% vs 31.1%, respectively; P <0.001) and anti-TNF-IR (50.0% vs 24.1%; P <0.05) subjects. Improvements with secukinumab 150 mg were observed for all secondary endpoints in anti-TNF-naive subjects, except ASAS partial remission, and for most secondary endpoints in anti-TNF- IR subjects. Clinical responses to secukinumab were sustained or continued to improve in both anti-TNF-naive and anti-TNF-IR subjects through 52 wks of therapy.
Conclusions: Secukinumab 150 mg s.c. provided sustained improvement in the signs and symptoms of AS, with associated reduction in inflammation and improvement in physical function and health-related QoL in both anti-TNF-naive and anti-TNF-IR subjects.

Reference

1 Sieper J, et al. Arthritis Rheumatol. 2014;66(11 Suppl):S232

P 15

Immediate response of therapy-refractory palmoplantar pustular psoriasis and psoriasis arthritis to tofacitinib

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Background: Palmoplantar pustular psoriasis (PPPP) is a difficult to treat variant of psoriasis. Here we present a case of successful treatment of PPPP and psoriasis arthritis with tofacitinib/Xeljanz.
Case presentation: A 61 years old female patient had her first manifestation of plaque psoriasis at the age of 15. At the age of 30 psoriasis arthritis was diagnosed, at 55 years an immobilizing PPPP. Both the arthritis and the skin lesions were refractory to sequential therapies with methotrexate, adalimumab, infliximab, PUVA therapy, oral acitretin, ustekinumab, glucocorticoids, NSAIDs. In march 2015 the patient suffered from severe pain in both wrists, shoulders, knees, several finger joints and the first toe left, synovitis of the finger joints and the toe (dactylitis), morning stiffness >2 hours, a patient-reported joint pain of 100 mm at the VAS scale. The PPPP was active, so that the patient was significantly limited in walking. CRP was 54 mg/l, the DAS28-CRP 5.86 (high activity). Based on the positive experience in rheumatoid arthritis and plaque psoriasis [1] we started an *off-label* therapy with 5 mg tofacitinib twice daily.
After only 7 days of treatment, the patient reported a spectacular improvement of joint pain and loss of morning stiffness. Both, pain intensity and impairment of general health dropped to 20 mm on the VAS, CRP decreased to 7.3 mg/l within 1 week, to <3 mg/l within 6 weeks. The DAS28-CRP was 2.39 and 2.16, respectively. The plantar skin lesions also improved rapidly, after only one month they had cleared completely. Prednisolon could be reduced immediately and stopped within 3 weeks, no pain medication was needed anymore. The astonishing result has sustained for more than 14 month until today. Dosage of tofacitinib had not to be increased. No side effects have occurred so far.
Conclusion: To our knowledge this is the first report on the effect of tofacitinib on PPPP with psoriasis arthritis. Tofacitinib appears to be a promising, easy to apply, well tolerated therapy in severe cases of PPPP and of psoriasis arthritis refractory to other therapies. A rapid approvel would be desirable. The stunning improvement in our patient could be due to the fact that tofacitinib targets a bunch of relevant cytokines.

Reference

1 Bachelez H et al., Lancet 2015

P 16

It is possible to predict which patients treated with biologic agents for rheumatic diseases will develop anti-drug antibodies?

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Introduction: All biologic agents (bDMARDs) currently used in rheumatology can induce anti-drug antibodies (ADAB), which will influence the drug levels and the drug effectiveness. Why only certain patients develop these antibodies is not yet clear, although there is already some literature dealing with anti-drug antibodies and trough drug level in rheumatic diseases.The aim of this study was to look for predictive factors of occurrence of such antibodies.
Methods: Since March 2013, we measure ADABs and trough levels for all anti TNF agent and also for rituximab and tocilizumab. Half of all our patients under biologic treatments have been tested. The method used is a sandwich ELIS A. ADABs, trough and TNF levels can be measured simultaneously. The reproducibility and the cut-offs have been tested among patients exposed and non-exposed to the medication. Clinical predictors of ADABs development were analyzed: gender, age, duration of the disease type of disease, duration of treatment, type of treatment, co-medication, previous biologic agent. Biologic predictors were: though level, TNF level, CRP and ESR.
Results: 297 patients had at least one measurement of ADAB and drug through level up to January 2016.
All the patients with ADABs were exposed to the medication, except for 3 patients (specificity: 98%). In patients exposed to bDMARDs, ADABs were found respectively for infliximab in 46/106 (44%) pts, adalimumab: 10/60 (16%) pts, certolizumab: 2/4 (50%) pts, etanercept: 1/20 (5%) pts, golimumab: 4/34 (12%) pts, tocilizumab: 1/75(1%) pts, rituximab: 4/46 (8%) pts. When ADABS against several bDMARDs were tested. On univariate analysis, several clinical and biological factors were significantly predictive of ADABS. After multivariate analysis only two clinical factors and two laboratory parameters remained independently associated: MAB anti-TNF treatment (OR: 26), previous bDMARD (OR: 5.9) and High TNF trough level (OR:4.2) and undetectable through level (OR: 34).
Conclusion: In this large real world cohort of patients with rheumatological conditions requiring bDMARD therapy, either by anti TNF or other biological agents and tested for ADAbs at different time point of their treatments, the best predictors of the presence of ABABs were: previous exposure to another biologic agent, treatment by an MAB anti TNF agent, undetectable through level of the medication and elevated TNF levels.

P 17

Adalimumab in Patients with Active and Inactive Non-infectious Uveitis

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Objective: To assess efficacy and safety of adalimumab (ADA) in patients (pts) with non-infectious uveitis (NIU).

Subjects and Methods: Pts with NIU enrolled in two global double-masked trials, VISUAL 1 (V1; pts with active uveitis despite ≥2 weeks (wk) of prednisone (PS), 10–60 mg/d) and VISUAL 2 (V2; pts with inactive uveitis dependent on 10–35 mg/d oral PS, to maintain inactivity). Pts were randomized 1:1 to receive placebo (PBO) or ADA (80 mg wk 0, followed by 40 mg every other wk from wk 1 for ≤80 wks). In V1, all pts received a PS burst followed by taper to 0 mg by wk 15. In V2, PS taper to 0 mg was mandatory by wk 19. The primary endpoint was time to treatment failure (TF) at or after wk 6 (V1) or wk 2 (V2). Adverse events (AEs) were assessed.
Results: The intent-to-treat analyses included 217 and 226 pts from V1 and V2, respectively. Risk of TF was reduced by 43–50% in ADA-treated pts compared to PBO (V1: HR = 0.50, 95%CI. 0.36–0.70, p<0.001; V2: HR = 0.57, 95%CI, 0.39-0.84, p = 0.004). Median time to TF was 13 wks for PBO, 24 wks for ADA (V1) and 8.3 months for PBO, not estimable for ADA (>18 months, since >50% of pts did not achieve TF) (V2). ADA-treated pts had fewer TF criteria than PBO in both studies. Rates of AEs were similar between treatment groups.
Conclusions: ADA lowered the risk of uveitic flare or vision loss in pts with NIU. No new safety signals were observed with ADA treatment.
Disclosures: Shigeaki Ohno has served on advisory boards for AbbVie and Santen. Antoine P. Brezin has served on advisory boards and as a consultant for AbbVie. Glenn Jaffe has served as a consultant for AbbVie. Andrew Dick has served on advisory boards for AbbVie. Quan Dong Nguyen has served on the Scientific Advisory Board for AbbVie, Santen, XOMA, Bausch & Lomb, and chairs the Steering Committee for the VISUAL studies. Martina Kron, Alex Song, Anne Camez and Samir Tari are AbbVie employees and may hold AbbVie stock or options.
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P 18

Safety and efficacy of Tocilizumab as monotherapy or in combination with MTX in patients with active rheumatoid arthritis and inadequate responses to DMARDs and/or TNF inhibitors: Subanalysis of the Austrian and Swiss patients of the ACT-SURE study

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Objective: To analyse efficacy and safety of tocilizumab in patients with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) or tumor necrosis factor (TNF) inhibitors within the Austrian and Swiss patients of the ACT-SURE study.
Methods: Subanalysis of RA patients from Austria and Switzerland, who participated in the global phase IIIb, open-label, ACT-SURE study. Patients with an inadequate response to DMARDs or TNF antagonists were included into the study. They received 8 mg/kg of tocilizumab every 4 weeks during 20 weeks. csDMARD therapy could be continued as combination therapy with tocilizumab (Combi) or stopped leading to a tocilizumab monotherapy (Mono) depending on the treating physician's discretion. Patients were analysed in separate for patients treated in combination with one or two csDMARDs or as tocilizumab monotherapy.
Results: Overall, 107 (85 on Combi and 22 on Mono) patients were treated with tocilizumab. No differences in ACR20/50/70/90 responses were observed between treatment groups (Mono: 63.6%, 40.9%, 22.7%, and 18.2% vs Combi: 61.2%, 43.5%, 25.9%, and 10.6%). The percentages of patients achieving a reduction in HAQ >0.22 or achieving a HAQ-DI remission (<0.5) were comparable (Mono: 68.4%, 36.8% vs Combi: 64.6% 36.9%).
The frequencies of related adverse events (AEs) and related serious AEs were different between tocilizumab monotherapy (45.5% and 4.5%) and combination therapy (34.1% and 5.9%). Infections were more frequent in patients treated in monotherapy (45.5% vs 27.1%). However, serious infections were rare (Mono n = 0, Combi n = 4). Infusion reactions were more frequent in monotherapy patients (22.7% vs 12.9%). In total 4.7% (Mono 4.5%, Combi 4.7%) of the patients discontinued treatment because of AEs. I
Conclusion: Tocilizumab was similarly effective, when used as monotherapy or in combination with csDMARDs in a broad population of patients with rheumatoid arthritis. We attribute the discrepancies in the rates of AEs and serious AEs to the relatively low number of patients included into this subanalysis. However, despite these discrepancies the percentage of AEs leading to an early discontinuation of the study was similar and very low, leading to the conclusion that tocilizumab is safe in mono- and as combination therapy with csDMARDs.

P 19

Is information about the reason for previous biologics discontinuation useful to predict the effectiveness of a biologic with a different mode of action?

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Background: With more biological disease modifying antirheumatic drugs (bDMARDs) in rheumatoid arthritis (RA), switching between bDMARDs is becoming more frequent. Patients (Pts) discontinue bDMARDs for various reasons, including inadequate effectiveness (IE) and adverse events (AE). Observational data indicates that the reason for discontinuing a second TNF inhibitor is usually the same that led to the first TNFi discontinuation, suggesting that a change in bDMARD mode of action may be more favourable.
Objectives: To investigate the impact of specific reasons for discontinuing the previous bDMARD on the clinical response to abatacept (ABA), a bDMARD with a different mode of action.
Methods: This is a pooled observational database analysis of 10 prospective cohorts of RA pts treated with iv ABA. All pts with available information on the reason for discontinuation of the last bDMARD were included. Pts initiating ABA as a first bDMARD were excluded from the analysis. The predictor of interest was the reason for prior bDMARD discontinuation, categorized as IE, AE, or other. The primary endpoint was time to ABA discontinuation, defined as the time between drug initiation to last administration: 1) for any reason, and 2) specifically for AEs or IE. Cox regression was used to estimate hazard ratios (HRs) for drug discontinuation, adjusting for pts demographics, disease and treatment characteristics.
Results: Of the 2001 RA pts included, 1272 discontinued ABA during the 3639 patient- years of follow-up. 499 pts (24.9%) had stopped their last bDMARD for AEs, 1290 pts (64.5%) for IE, and 212 pts (10.6%) for other reasons.
There was no association between reason for discontinuing prior bDMARDs (AE, IE, or other) and overall ABA retention (log-rank p = 0.78). ABA discontinuation for AEs was significantly associated with prior discontinuation of bDMARDs for AEs (log-rank p <0.001), and ABA discontinuation for IE was significantly associated with prior bDMARD discontinuation for IE (log-rank, p = 0.02).
Conclusions: The same reason that led to discontinuing prior bDMARDs is likely to lead to the discontinuation of a new bDMARD with a different mode of action. Overall these results suggest that discontinuation is mostly explained by patientspecific characteristics (selection) and less by particular drug mechanism.
Acknowledgement: Unrestricted research grant from BMS.

P 20

Baricitinib versus placebo or adalimumab in patients with active rheumatoid arthritis and an inadequate response to background methotrexate therapy: Results of a phase 3 study

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Background: We report a 52-week, global, randomized study of baricitinib in patients with active rheumatoid arthritis (RA) and an inadequate response (IR) to background methotrexate (MTX).
Methods: Patients with active RA (TJC≥6+SJC≥6+hsCRP≥6mg/L) and background MTX received placebo, baricitinib 4mg QD, or adalimumab 40mg Q2W. At Wk24, placebo patients switched to baricitinib. Primary endpoint was Wk12 ACR20 response (baricitinib vsplacebo). Secondary endpoints included comparing baricitinib vs adalimumab for ACR20 and DAS28-CRP at Wk12 and baricitinib vs placebo for mTSS at Wk24.
Results: Of 1305 randomized patients, 83%, 88% and 87% completed Wk52 in placebo, baricitinib and adalimumab groups. Wk12 ACR20 response was higher for baricitinib vs placebo (70%vs 40%;p ≤.001). At Wks12/24, improvements in response rates, and low disease activity/remission rates, were significant for baricitinib vs placebo, as early as Wk1. Baricitinib was superior to adalimumab for measures including Wk12 ACR20 response and DAS28-CRP improvement. Wk24 mTSS change was lower for baricitinib vs placebo (0.41vs 0.90;p ≤.001). Patient-reported outcomes improved significantly in patients receiving baricitinib vs placebo, as early as Wk1. TEAE rates, including infections, were higher for baricitinib and adalimumab vs placebo. SAE rates were similar for baricitinib and lower for adalimumab vs placebo; serious infection rates were similar across groups.
Conclusions: Baricitinib produced significant clinical improvements vs placebo and adalimumab, with acceptable safety/tolerability profiles.

P 21

Short-term effectiveness of inpatient cancer rehabilitation: A longitudinal controlled cohort study

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Background: After having treated in acute hospital due to life-threatening cancer, patients often suffer from physical and mental consequences, which may prevent from living at home – independently from social support. Tissue-damage of cancer resection, metastases, and fatigue offer potential for musculoskeletal rehabilitation. The study aimed to examine and to compare bio-psycho-social health and quality-of-life of cancer patients after acute treatment admitted to inpatient rehabilitation (IR) or discharged at home with advice (A+) or without advice (A-) for inpatient rehabilitation by the treating physician.
Methods: This naturalistic, prospective, controlled cohort study used standardized outcomes: Short Form 36 (SF-36), Functional Assessment of Cancer Therapy (FACT), Hospital Anxiety and Depression Scale (HADS). Changes between discharge of acute hospital/start of rehabilitation (baseline) and 3 weeks later/end of rehabilitation (follow-up) were compared by standardized mean differences (SMD). SMDs were quantified by bivariate analysis and multivariate linear regression modeling controlling for potential confounders as sex, age, number of comorbidities, baseline state.
Results: In the comparison IR (n = 133) versus A+ (n = 30), effect differences attained SMD bivariate/SMD multivariate: 0.62/0.62 on SF-36 Physical functioning, 0.48/0.37 on SF-36 Bodily pain, 0.53/0.70 on SF-36 Social functioning, 0.61/0.54 on FACT fatigue, 0.62/0.53 HADS Depression, 0.28/0.37 on HADS anxiety. In the comparison IR (n = 133) versus A- (n = 82), effect differences attained SMD bivariate/SMD multivariate: 0.28/-0.06 on SF-36 Physical functioning, 0.10/0.06 on SF-36 Bodily pain, 0.33/0.10 on SF-36 Social functioning, 0.66/0.29 on FACT fatigue, 0.37/0.15 HADS Depression, 0.14/0.07 on HADS anxiety.
Conclusions: The comparison between inpatient rehabilitation and discharge to home despite advice for inpatient rehabilitation showed moderate, statistically significant effects, which remained stable after controlling for confounders. In contrast, the comparison between inpatient rehabilitation and discharge to home without advice for inpatient rehabilitation showed small, statistically not significant effects, which disappeared after controlling for confounders. Inpatient cancer rehabilitation can be recommended as effective management, preconditioned careful indication for the need of rehabilitation after initial acute treatment.

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P 22

Differences in the course of Italian- and German-speaking patients' outcome after interdisciplinary pain program

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Background: The aim of this study was to quantify state and changes of health state and quality of life of native Italian-speaking patients with fibromyalgia or chronic back pain before and after a 4-week, interdisciplinary inpatient pain program and to compare the results with native German-speaking patients.
Methods: The prospective cohort study with 62 Italian-speaking and 63 German-speaking patients measured health-related quality of life, pain, fear and depression comparing at baseline, after 4 weeks of pain program and at 1 year follow-up. Differences between the two groups were tested on significance by generalized estimation equations (GEE). This method modeled changes of health by multivariate logistic regression adjusting for sex, education, number of comorbidities and the baseline score over both follow-ups for each scale.
Results: Italian-speaking patients (n = 62) showed higher proportions of males, lower educated and less burdened by comorbidities than German-speaking patients (n = 63). At baseline, physical and psychosocial health, depression and fear of the Italian-speaking patients were worse than German-speaking patients, with the exception of less pain in the Italian-speaking patients on the SF-36. Changes of health showed more improvement in German- than in Italian-speaking patients on all scales and at both follow-ups. In GEE, the highest differences were observed in SF-36 physical functioning (p = 0.036), HADS anxiety (p = 0.031) and HADS depression (p = 0.017). On SF-36 bodily pain the difference was not significant (p = 0.142).
Conclusions: This study detected that short- and midterm outcome of Italian-speaking patients was worse than that of German-speaking patients, even after adjustment for baseline differences. The reasons for that are unclear and may have consequences for future management of Italian-speaking patients in interdisciplinary pain management programs. This supports the hypothesis that patients with migration background may have special needs in therapeutic management.

P 23

To investigate the effectiveness of different conservative interventions for pain, shoulder function and active range of motion in adults with shoulder impingement

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Objective: To investigate the effectiveness of different conservative interventions for pain, shoulder function and active range of motion in adults with shoulder impingement.
Design: Systematic review and meta-analysis of randomized controlled trials.
Data sources: Systematic searches in Medline, CENTRAL, CINAHL, Embase, and PEDro up to November 2015 and hand searches of reference lists and forward citation tracking of included trials.

Study selection criteria: Randomized trials published in full text including adult participants with shoulder impingement and evaluating at least one conservative intervention against sham or active treatments.
Results: One hundred eighty-three trials including a total of 11039 participants. For the outcome pain at the longest follow-up, there was but very low quality evidence that exercise had a large standardized mean difference (SMD) of –0.94 with a 95% CI from –1.69 to –0.19 compared to doing nothing while specific exercises were better than generic exercises with a SMD of –0.54 (–0.79 to –0.28). Corticosteroid injections showed a large SMD of –0.65 (95% CI –1.04 to –0.26) compared to no treatment, while ultrasound guided injections were better than non-guided –0.66 (95% CI –1.21 to –0.10). For NSAIDS had a small to moderate SMD of –0.29 (95% CI –0.53 to –0.05) was found. Manual therapy was better than placebo (SMD = –0.46 (95% CI from –0.88 to –0.08)) and manual therapy plus exercise was non-significantly better than exercise alone –0.24 (95% CI –0.60 to 0.12). Laser had a large SMD of –0.88 (95% CI –1.48 to –0.27) compared to exercise and –0.65 (95% CI –1.24 to –0.06) compared to sham laser. Extracorporeal shockwave therapy was better than sham therapy with a small to moderate SMD of –0.39 (95% CI –0.78 to –0.01). Tape plus exercise was better than physiotherapy (SMD = –0.45 (95% CI –0.80 to –0.09)).
Conclusion: Although there was only very low quality evidence, general and specific exercises should be prescribed for patients with shoulder impingement symptoms. Tape, laser or manual therapy might be added to exercise. NSAIDS can be recommended if necessary. Corticosteroid injections might only be recommended when exercise or other modalities are not possible. If corticosteroid injections are applied, they should be provided under ultrasound guidance.

P 24

Long-Term Effectiveness of the Bern Ambulatory Interprofessional Rehabilitation (BAI-Reha) for patients with chronic musculo-skeletal pain: a cohort study

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Aim: The aim of this study was to evaluate the short-, medium-, and longterm effectiveness of the Bern Ambulatory Interprofessional Rehabilitation (BAI-Reha) program for patients with chronic musculoskeletal pain.
Methods: We collected data at baseline, after 3 months (at the end of the program), after 1 and 2 years on work proportion, quality of live (EuroQoL), pain intensity (NRS, Numeric Rating Scale), burden of suffering (PRISM, Pictorial Representation of Illness and Self Measure), self-rated and observed quality of and satisfaction with daily life task performance (AMPS, Assessment of Motor and Process Skills; COPM, Canadian Occupational Performance Measure).
We implemented mixed-model analyses and estimated effect sizes for significant and clinical meaningful differences among means at baseline, at the end of the program, and at 1-year-follow-up and 2-year-follow-up.
Results: 30 consecutive patients with chronic musculoskeletal pain, aged between 20 and 73 (*M* 44.83; *SD* 12.57) were included. We found significant intervention effects between means at baseline and post intervention in work proportion [*CI* 8.94,30.39], pain intensity [*CI* 3.57,6.08], quality of life [*CI* .58, .79; 50.05, 65.13], burden of suffering [*CI* 6.98, 13.24], self-rated and observed quality of and satisfaction with daily life task performance [*CI* ≥1.23, ≤6.43]. The intervention effects remained stable or increased among means at post-intervention, 1-year-follow-up and 2-year-follow-up evaluations, except quality of life. Effect sizes were moderate to large (*d* = .53–1.85) among evaluation times except quality of life index and pain intensity. Mixed-model analyses revealed significant time effects over two years for work proportion (*F* = 5.06, *df* = 43.103, p <.01) and non-significant time effects for the other outcomes (*F* ≥.59, *df* ≥28.37, p≥.20).
Conclusions: The BAI-Reha is effective for patients with chronic musculo-skeletal pain. The beneficial effects remain stable or improve over at least two years post intervention.

P 25

Establishing a prospective pregnancy registry within SCQM to study the interaction of pregnancy, rheumatic diseases, anti-rheumatic therapy and the offspring's health status

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Rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) can affect women of the reproductive age. For these women family planning is an important issue in their life. However disease activity and medication can have an influence on fertility and pregnancy outcome. On the other hand, pregnancy can influence disease activity. Until now, most studies have been performed in RA patients before the era of biologic therapy whereas very few data exist in PsA and axSpA.
The aim of this project is to establish a prospective pregnancy registry within the SCQM registry to prospectively collect national data on women with RA, axSpA and PsA before, during and after pregnancy. A SCQM pregnancy registry will not only help to standardize the monitoring of pregnant patients with RA, axSpA and PsA but also allow to study the interaction of pregnancy, rheumatic diseases, anti-rheumatic therapy and the offspring's health status in a national context.

P 26

Salutogenic concepts in the rehabilitation of osteoarthritis

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Background: The treatment strategies for osteoarthritis (OA) are well known from numerous studies. One of the challenges is long-term patient compliance to the recommended therapies without supervision.
Objective: To examine the ability of salutogenic concepts to improve rehabilitative management of OA.
Materials and methods: Review article introducing salutogenic concepts and their empiric evidence, focussing on Antonovsky's sense of coherence (SOC).
Results: The SOC consists of the three component scomprehensibility, manageability and meaningfulness. SOC can be quantified by SOC-13, a self-reported measurement with 13 items. Associations of the SOC with different dimensions of health (in particular with Short Form 36, SF-36) are known from cross-sectional studies. Most studies showed a stronger correlation of the mental than the physical health dimensions of SF-36 with SOC-13. This result is consistent with baseline examinations of hip and knee OA patients before rehabilitation. At the 6-month follow-up, correlations between SOC and the changes of the SF-36 scores were weak. A salutogenically orientated instruction for self-management of symptoms in cancer patients showed significant improvement in SOC.
Conclusion: Increasing SOC can lead to health improvements on many levels, e.g., self- efficacy, reduction of fear, coping, education, resources and compliance to treatment. Empirical proof that interventional measures increasing SOC can improve the health of OA patients is currently unavailable.

Reference
Z Rheumatol. 2015;74(7):597–602.

P 27

Gout tophus detection – A comparison of dual-energy CT(DECT) and histology

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Objectives: To compare dual-energy CT images (DECT) directly with gold standard histology.
Methods: A 85-year-old woman with chronic recurrent gouty arthritis and macroscopically visible tophi was assessed with DECT-scans of her feet .When she died 7 days later, three tophi in different regions and in different tissues of her left foot were processed for histological examination.
Results: Of the selected tophi, two were almost completely missed by the color-coding DECT sequences. The tophi remained in most of their volume below the detection threshold value of 150HU(default value).
Conclusions: It could be demonstrated that DECT only highlights the dense tophi (corresponding of approximately 15–20 vol%urate in the tophus). Less dense tophi,despite considerable size, will be missed in the color-coded images.

P 28

Immediate and long term efficacy of Kineret in acute shoulder syndrome due to hydroxyapatite calcification of the rotator-cuff: real-life experience of 10 cases

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Background: Acute shoulder syndrome is due to acute inflammation linked to the dissolution of hydroxyapatite calcification in the tendon or the bursa of the shoulder. Usually self- limited, can last up to two weeks with very intense pain and limitation of the function. Steroid and trituration have been proposed to shorten the duration of the flare. We have published a pilot study of the beneffits of Kineret in the situation showing a rapid solution of pain within a day and recovery of mobility after 3 days, without evaluation of long time effect on pain and relapses.
Aim of the study: Evaluation of the immediate and long time effect of 3 injections of Kineret in real life condition.
Methods: A retrospective study of all 10 patients who have received Kineret in the last five years for acute shoulder syndrome due to calcific periarthritis because of no response to NSAIDs Immediate evolution based on clinical data of charts: pain on day 0 and day 3 after Kineret, x-ray, ultrasound and inflammatory parameters day 0 and within one week after Kineret. The long time evolution based on clinical data on charts and phone calls to the patients: new relapses, residual pain, US and X-ray evolution and other manifestations of apatitis arthropahies.
Results: In 8 patients of 10 included, the flare was very acute and not preceded by chronic shoulder pain or previous self limited flare. In two patients, the flare was preceded by chronic pain and at least one previous flare. The immediate beneffit of kineret was spectacular for pain, function and inflammatory parameters in all patients(table1). In none of the patients, calcification disappeared completely after the treatment (within 4 W).

Table 1: Clinical and demographic characteristics of the 10 patients.

Age median	VAS initial	VAS day 3	VAS residual	CRP initial	CRP day 3	VS initial	VS day 3
57 y	8.8/10	2/10	3.5/10	35 mg/l	12 mg/l	41 mm/h	34 mm/h

The mean follow-up was 32 months. 4 acute relapses were reported only by 2 patients who have already chronic shoulder pain and previous flares. Mild chronic pain are present in 4 patients more in relation with some other coexisting joint pathology. Other manifestations of apatite's arthropathy occurred in 1 of relapsing patients.
Conclusions: Kineret is an interesting therapeutic approach in acute calcific periarthritis in patients non responding to NSAIDs. The effect on pain is strong and occurs within 3 days. Only 2 patients presented relapses.

P 29

Quantity and quality of bone in patients with Osteogenesis Imperfecta measured by DXA (BMD and TBS): correlation with genotype and fracture risk

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Osteogenesis Imperfecta (OI) is a rare genetic disease caused by a defect in type I collagen or in proteins that interact with it. Recent knowledge regarding the genetics of OI allows an accurate diagnosis of the specific type of OI and its molecular mechanism. If the fracture risk is high, medications against osteoporosis are usually proposed. Some are more efficient on bone quantity and others on bone quality or both. In this study we evaluated the bone quantity by DXA and the bone quality by Trabecular Bone Score (TBS) and analyzed their relation with fracture risk, phenotype and genotype for 31 OI adult patients.
Method: Retrospective study of 31 adult patients with OI. BMD was measured at the femoral neck (FN), the total hip (TH) and the spine (LS). TBS was analyzed by the means of DXA images of the LS. BMD and TBS results were expressed in T score and means respectively, for the entire study population for comparison with the normal population and separately for the genotype and phenotypes subgroups.
Results: 31 patients, 21 women, 10 men, mean age 40 ± 14 years. Phenotypes: 21 type I, 7 type III, 3 type V. Genotypes: 9 *COL1A1,* 6 *COL1A2,* 3 *IFITM5* mutations. Mean age of the first fracture was 4 ± 2 years. 26 patients had multiple fractures. Mean BMD T-score were: FN –1.83 ± 1.19, TH –1.5 ± 1.11, LS –2.77 ± 1.30. Mean TBS was 1.25 ± 0.13. For this young population, all results were lower than the normal population (1.48 ± 0.09, normal TBS). Comparison between the phenotypes: no difference between type I and III regarding the LS BMD (–2.8 vs –3.0, p = 0.6) but TBS was significantly lower for type III compared to type I (1.16 vs 1.27, p = 0.03). Comparison between type III and V: same results. Comparison between the genotypes: LS BMD and TBS were lower in *COL1A2* patients compared to *COL1A1* patients (–4.15 ± 0.44 vs –2.8 ± 0.5, p = 0.04, and 1.15 ± 0.03 vs 1.29 ± 0.14, p = 0.02). No difference was found for TH and FN.
Conclusion: in our group of 31 OI adult patients, we found that all measurements of bone health (BMD and TBS) are lower than in the normal population. We can distinguish OI types I, III and V based on the TBS measurement with the lower values for the type III and the higher values for the OI type V. Patients with *COL1A2* mutation had the lower TBS and LS BMD. This knowledge could help the clinician in the choice of the best treatment.

P 30

Patients with osteogenesis imperfecta disease walk with reduced ground reaction force compared to healthy subjects

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Osteogenesis Imperfecta (OI) is characterized by a decreased osseous density and an increased fracture risk. Hyperlaxity and muscle weakness are also common. Treatment is multidisciplinary, medical (bisphosphonates), surgical and functional. Assessing the physical capacity of OI patients is important to evaluate disease progression and to adapt treatment, specifically rehabilitation protocol. While functional scores, such as the MOS SF-36 or the Oswestry Disability Index are validated and used to assess physical capacity in this population, instrumented gait test could improve the evaluation. Unfortunately, using a full gait lab is too cumbersome for routine practice. Analyzing ground reaction forces (GRF) during walking, which can be done with a single force plate, was shown to be an easy and efficient method to differentiate ambulatory pattern in relation to disease severity for a variety of musculoskeletal pathologies. The objective of this study was to compare GRF during the stance phase of walking between a group of OI patients and a control group. Gait analysis was performed for 6 OI patients (2 males; 27 ± 9 yo) and 12 healthy subjects (7 males; 24 ± 2 yo). Each study participant walked several trials at self-selected normal speed in a lab equipped with floor-mounted forceplates (Kistler, CH). One leg was randomly selected for analysis and standard characteristic peaks in vertical and fore-aft GRF were measured for each step of the selected leg on a forceplate. To allow comparison among participants GRF were normalize to percent bodyweight (%BW).Compared to the controls, OI patients walked with significantly reduced vertical GRF during loading response (88 ± 19 vs 114 ± 8 %BW; p <0.001) and during terminal stance (89 ± 14 vs 109 ± 9 %BW; p <0.001). The magnitude of the GRF was different in the horizontal plane, with reduced aft force during loading response (17 ± 6 vs 23 ± 5 %BW; p = 0.03) and reduced fore force during terminal stance (17 ± 3 vs 22 ± 4 %BW; p = 0.01). OI patients walked slower than controls (1.22 ± 0.14 vs 1.47 ± 0.20 m/s; p = 0.02). Smaller GRF were hypothesized due to muscle weakness, proprioceptive acuity diminution and fear of falling. These expected results suggest that a single force plate can already provide valuable information to characterize the ambulatory function of OI patients. Further study is needed to evaluate specific change in GFR among OI patients with functional treatment.

P 31

Epidemiology of back pain in young Swiss adults: a longitudinal population cohort survey from age 27 to 50 years

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Background: Back pain is the most prevalent and most burdening disorder for individual and public health. The aim was to determine prevalences and incidences of lumbar and cervical back pain over a course of 23 years and to quantify associations to concomitant disorders.
Methods: Data from the well-known Zurich study collected between 1986 and 2008 about lumbar, cervical back pain, and mental disorders were analyzed. Epidemiologic parameters were back-weighted to obtain representative rates for the canton of Zurich representing 1/6 of the Swiss population. Associations were quantified by odds ratios (OR).
Results: Of n = 499 subjects, 68.9% ever experienced lumbar and 60.7% cervical back pain, corresponding to 23-year prevalences of 66.9% and 54.9% and 23-year incidences of 52.3% and 48.9% for lumbar and cervical. Annual prevalences varied by 28.4–47.2% for lumbar and 18.3-54.7% for cervical back pain; the corresponding annual incidences by 5.8–13.3% and 7.8–12.6%. Lumbar back pain was significantly associated with cardiovascular diseases (OR = 4.59), obesity (OR = 3.98), asthma spectrum (OR = 5.74), tranquilizer dependence (OR = 5.85), and other comorbidities (OR: 1.47 to 3.27). Significant associations to cervical back pain were observed for specific phobia (OR = 5.10), panic attacks (OR = 4.79), and other comorbidities (OR: 1.61 to 2.62).
Conclusion: This study contributes to refine epidemiologic data about lumbar and cervical back pain, representative for the biggest canton of Switzerland. Some associations to treatable concomitant disorders were high. That may offer possibilities for indirect management of lumbar and cervical back pain relief.

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Is there an optimal TBS lumbar spine vertebrae combination to predict major Osteoporotic Fracture? The OsteoLaus Cohort Study

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Introduction: The international guidelines recommend to use the average bone mineral density (BMD) over L1 to L4 in the management of osteoporosis and prediction of fracture. Exclusion of certain vertebrae is recommended according to specific rules (ISCD position). The spine Trabecular Bone score (TBS), a surrogate of bone micro-architecture, has been newly introduced into international guidelines and the FRAX® tool for clinical use in conjunction with BMD and clinical risk factors. The aim of this study is to test several TBS vertebrae combinations in regard to major osteoporotic fracture prediction.
Methods: The osteoLaus cohort (Lausanne, Switzerland) included 1500 woman 50 to 80 years old. All women had a detailed questionnaire related to clinical risk factors and treatment known to influence bone metabolism, BMD measurement (hip, spine and whole body), vertebral fracture assessment and TBS. The primary outcome was the prevalence of major osteoporotic fracture (MOF) according to TBS per-vertebral combination. Appropriate statistics and necessary adjustment for confounding factors were performed. L1-L4 TBS was used as reference value.
Results: Out of 1466 women included in the study (mean age 64.5 ± 7.6 years, BMI 25.7 ± 4.4), 12.7% suffered from MOF. The odd ratios per standard deviation decreased (OR) were 1.53 (1.29–1.80) and 1.80 (1.50–2.15) for the spine and total femur BMD respectively. Adjusted (age & glucocorticoids status) OR and area under the curve (AUC) of different combination of vertebrae can be found in the following:
Combination L1-2 TBS: OR = 2.16 (1.80–2.58) and AUC = 0.73 (0.69-0.76), p vs L14TBS and p vs L12TBS: ns. L1-3 TBS: OR= 2.09 (1.74–2.50), AUC = 0.72 (0.68–0.75): ns. L1-4 TBS: OR = 1.98 (1.65–2.36), AUC = 0.71 (0.67-0.75): ns. L2-3 TBS: **OR = 1.92** (1.61–2.29), AUC = 0.70(0.66–0.74): **p = 0.04 vs L12TBS**. L2-3 TBS: **OR = 1.81** (1.52–2.17) and AUC = 0.69 (0.65–0.73): **p <0.001 vs L14BS and p <0.001 vs L12TBS.** L3–4 TBS: **OR = 1.53** (1.29–1.82) AUC = 0.68 (0.65–0.72), **p = 0.0002 vs L14BS and p = 0.0002 vs L12TBS.**
Further analyses are under process on other types of fracture and will be reported.
Conclusion: It seems that excluding L4 tends to improve the fracture risk prediction. TBS is very sensitive to vertebra positioning (e.g. projection). To compensate for the natural lordosis of the spine, one has to lift the legs of the patient. L4 is often still angled which could explained such results. Further prospective studies are needed to confirm these results.

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Decrease of bone mineral density and occurrence of new vertebral fractures after stopping Denosumab

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Introduction: Denosumab (Dmab) has been demonstrated in clinical trials to be very effective in improving bone mineral density (BMD) and reduce osteoporotic fractures. Therefore it is increasingly used to treat osteoporotic patients also in clinical practice. However, like in bisphosphonates, cases of atypical femoral fractures (AFF) and osteonecrosis of the jaw (ONJ) were reported under Dmab treatment. Thus, a life-long therapy with Dmab – as in bisphosphonates – might not be appropriate. Moreover, when given as prophylaxis in patients under aromatase inhibitor (AI) therapy, Dmab is only reimbursed for the time of AI-therapy in Switzerland. As Dmab has been introduced into the Swiss market in 2010, it is likely that many patients will stop Dmab in the next years or have already stopped therapy. However, there is an increasing number of cases reported in the literature, where severe new vertebral fractures occurred and BMD decreased dramatically within a few months after stopping Dmab. Given the high number of treated patients who may be taken off the drug in the next few years it is essential to know this possible outcome and to develop strategies against the loss of BMD and occurrence of vertebral fractures after stopping Dmab. We report 6 cases of patients who had received Dmab during the pivotal FREEDOM study for 7 and 10 years, respectively and were taken off Dmab when the study was completed. All of them sustained either a massive decrease in BMD or had new vertebral fractures.
Patients: All patients were included in the FREEDOM-trial. One patient received Dmab for a total of 10 years; the other 5 patients were treated for 7 years. In all patients, BMD of the lumbar spine **increased** between 10.1% and 30.8% during the treatment. One year after having stopped Dmab BMD had **decreased** between 3.2% and 17.8% at the lumbar spine. Two patients had sustained vertebral fractures (T 10/ 11 and L 4/ 5, resp.).
Conclusion: The data of these 6 patients confirm previous reports on a decrease of BMD and occurrence of new vertebral fractures after Denosumab therapy is stopped. Hence, treating physicians should be informed about this issue and a strategy is needed to overcome the high risk of new vertebral fractures a few months after stopping Denosumab.

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Classification criteria for lumbar radicular pain due to disk herniation

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Background: Imaging evidence of lumbar disc herniations (DH) may not be associated with symptoms, therefore classification criteria based upon patient symptoms and physical examination findings are required. This study sought to develop a set of criteria identifying patients with radicular pain (RP) caused by LDH and patients with neurogenic claudication (NC) caused by LSS. Results concerning RP caused by LDH are reported.
Methods Phase 1: 17 spine specialists from 8 countries participated in a Delphi process, using an internet program, to rank symptoms and signs which suggest LDH as the cause of RP or LSS as the cause of NC. Phase 2: 18 different spine specialists recruited patients and classified them with a high degree of confidence as having either: 1) RP due to LDH, 2) neurogenic claudication (NC) due to LSS, or 3) non-specific low back pain (NSLBP) with non-specific leg pain radiation. Patients completed survey items and specialists documented examination signs. Signs and symptoms present in ≥ 10 patients were analyzed by using Generalized Estimating Equations (GEE). Patients with NC due to LSS or NSLBP served as controls. Items with p <0.1 in univariate analysis were entered in the multivariate analysis. A score to predict RP due to DH was developed based on the coefficient of the GEE, and used to obtain a ROC curve and the associated area under the curve (AUC).
Results: A list of 46 clinical signs and 28 patient-reported symptoms were selected by the group of spine specialists during the 1st phase. For the 2nd phase, 209 patients with high confidence in the diagnosis were included, 89 RP due to DH, 63 NC, and 57 NSLBP with non-specific leg pain radiation. Items which predicted RP with a p-value <0.1 included monoradicular pain, leg pain not decreased when sitting, positive straight leg raising test <60°, unilateral motor weakness and asymmetric ankle reflex. The score had an AUC of 0.92, and the cutoff to obtain a specificity of >90% resulted in a sensitivity of 70.4%.
Conclusion: An international collaboration of surgeon and non-surgeon spine specialists produced a set of diagnostic criteria with high specificity and sensitivity for identifying patients with RP caused by DH. Using this set could improve the quality of basic science and clinical research in this field by improving homogeneity within groups of patients.

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Classification criteria for neurogenic claudication caused by lumbar spinal stenosis

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Background: Since imaging evidence of lumbar spinal stenosis (LSS) or lumbar disc herniations (LDH) may not be associated with symptoms, classification criteria based upon patient symptoms and physical examination findings are required. This study sought to develop a set of criteria identifying patients with neurogenic claudication (NC) caused by LSS and patient with radicular pain (RP) caused by LDH Results concerning NC caused by LSS are reported.
Methods Phase 1: 17 spine specialists from 8 countries participated in a Delphi process, using an internet program, to rank symptoms and signs which suggest LSS as the cause of NC or DH as the cause of RP. Phase 2: 18 different spine specialists (surgeons and non-surgeons) recruited patients during office visits and classify them with a high degree of confidence as having with either: 1) NC caused by LSS 2) RP caused by LDH or 3) non-specific low back pain (NSLBP) with non-specific leg pain radiation. Patients completed survey items and specialists documented examination signs. Signs and symptoms present in ≥10 patients were analyzed by using Generalized Estimating Equations (GEE). Patients with NC caused by LSS or NSLBP served as controls. Items with p <0.1 in univariate analysis were entered in the multivariate analysis. A score to predict NC caused by LSS was developed based on the coefficient of the GEE, and used to obtain a ROC curve and the associated area under the curve (AUC).
Results: A list of 46 clinical signs and 28 patient-reported symptoms were selected by the group of spine specialists during the 1st phase. For the 2nd phase, 209 patients with high confidence in the diagnosis were included 63 NC caused by LSS, 89 RP caused by DH, and 57 NSLBP with non-specific leg pain radiation. Items which predicted NC with a p-value <0.1 included age >60, bilateral leg pain, leg pain relieved by sitting, leg pain decreased by leaning or flexing, positive30 seconds extension test, negative straight leg raise test. The score had an AUC of 0.91, and the cutoff to obtain a specificity of 92.1% resulted in a sensitivity of 80.0%.
Conclusion: An international collaboration of surgeon and non-surgeon spine specialists produced a set of diagnostic criteria with high specificity and sensitivity for identifying patients with NC caused by LSS. Using this set could improve the quality of basic science and clinical research in this field by improving homogeneity within groups of patients.

The numbers refer to the pages of this supplement.