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FM 1

Anti-Apolipoprotein A-1 IgG Predict Major Cardiovascular Events in Patients with Rheumatoid Arthritis

Nicolas Vuilleumier[1], Sylvette Bas[1,2], Sabrina Pagano[1], Fabrizio Montecucco[3], Pierre-André Guerne[2], Axel Finckh[2], Christian Lovis[4], François Mach[3], Denis Hochstrasser[1], Pascale Roux-Lombard[5], Cem Gabay[2,6]
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Objective: To determine whether anti-apolipoprotein (apo) A-1 IgG are associated with major cardiovascular events (MACE) in rheumatoid arthritis (RA) patients.
Methods: We determined anti-apoA-1 IgG levels and the concentrations of cytokines, oxidised low density lipoprotein (oxLDL) and metalloproteinases (MMPs) 1, 2, 3, 9 in the sera of 133 RA patients without cardiovascular disease at baseline, who where all longitudinally followed over a median period of nine years. MACE was defined as fatal or non-fatal stroke or acute coronary syndrome. The pro-inflammatory effects of anti-apoA-1 IgG were assessed on human macrophages *in vitro*.
Results: During follow-up, overall MACE incidence was 15%. At baseline, anti-apoA-1 IgG positivity was 17% and was associated with a higher MACE incidence (adjusted Hazard Ratio: 4.2; 95%CI: 1.5–12.1). Patients with subsequent MACE had higher circulating levels of anti-apoA-1 IgG at baseline (p = 0.001). ROC curve analysis showed that anti-apoA-1 IgG was the strongest predictor of all tested biomarkers for subsequent MACE with an area under the curve of 0.73 (p = 0.0008). Anti-apoA-1 IgG positivity was associated with higher median circulating levels of IL-8 (p = 0.01), oxLDL (p = 0.02), MMP-9 (p = 0.03), and higher pro-MMP-9 activity as assessed by zymography (p = 0.008). On human macrophages, anti-apoA-1 IgG induced a significant dose-dependent increase of IL-8 and MMP-9 levels, and pro-MMP-9 activity.
Conclusion: Anti-apoA-1 IgG is an independent predictor of MACE in RA, possibly by affecting atherosclerotic plaque vulnerability.

FM 2

Canakinumab (ACZ885) vs colchicine in the prevention of flares in gouty arthritis patients initiating allopurinol therapy

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Aim: This study compared canakinumab (a fully human anti-IL-1β antibody) vs colchicine in preventing flares in gouty arthritis patients initiating allopurinol therapy.
Methods: In this 24-week, multi-center, double-blind, double-dummy study, 432 gout patients aged 20–79 years initiating allopurinol were randomized (1:1:1:1:1:1:2) to canakinumab subcutaneous (sc) single doses of 25, 50, 100, 200, 300 mg, or 150 mg divided in doses every 4 weeks (50+50+25+25 mg [q4wk]) or 16 weeks colchicine 0.5 mg daily. Herein, we report the efficacy and safety results of a pre-planned interim analysis after all patients have completed the 16 weeks efficacy part of the study. The primary objective was to determine the canakinumab dose giving comparable efficacy to colchicine with respect to the number of gout flares occurring during first 16 weeks.
Results: 432 patients were randomized; 38 patients (7–11% of each study group) had discontinued the study at the interim analysis timepoint. All canakinumab doses were better than colchicine in preventing flares and therefore a canakinumab dose comparable to colchicine was not found. All canakinumab groups reduced the event rate significantly compared to colchicine based on the negative binomial model (rate ratio estimates 25 mg 0.52, 50 mg 0.34, 100 mg 0.25, 200 mg 0.40, 300 mg 0.29, q4wk 0.38; p ≤0.05 for all). The percentage of patients with flares was lower for all canakinumab groups (25 mg 23.6%, 50 mg 16.7%, 100 mg 13.5%, 200 mg 20.4%, 300 mg 15.4%, q4wk 17.0%) compared to colchicine 43.9% (p ≤0.05 for all). All patients taking canakinumab were significantly less likely to have flares than patients taking colchicine (odds ratio range [0.20–0.39]; *p* ≤0.05 for all). Adverse events occurred in 45.5% (25 mg), 44.4% (50 mg), 48.1% (100 mg), 46.3% (200 mg), 50.9% (300 mg), and 58.5% (q4wk) of patients on canakinumab vs 51.9% of patients on colchicine. Serious adverse events were reported in 2 (3.6%; 25 mg), 2 (3.7%, 50 mg), 2 (3.7%, 100 mg), 3 (5.6%, 200 mg), and 1 (1.9%, q4wk) patients on canakinumab and in 6 (5.6%) patients on colchicine. One fatal myocardial infarction occurred in the colchicine group.
Conclusion: In gouty arthritis patients initiating allopurinol therapy, treatment with canakinumab led to a statistically significant reduction in flares compared with colchicine, and was well tolerated.

FM 3

Octacalcium phosphate (OCP) crystals induce inflammation in vivo through IL-1 but independent of the NLRP3 inflammasome

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Introduction: We determined the mechanisms involved in the murine inflammatory response to OCP crystals in vivo.
Methods: OCP crystal-induced inflammation was monitored using the peritonitis model of inflammation. The production of IL-1α, IL-1β and myeloid-related protein (MRP) were determined by ELISA. Peritoneal neutrophil recruitment was determined by flow cytometry. Depletion of resident macrophages or of mast cells was performed by pretreatment with clodronate liposomes or with compound 48/80, respectively.
Resuls: OCP induced a strong inflammatory response with marked neutrophil influx and up-regulation of IL-1α, IL-1β, and MRP in the peritoneal cavity. This OCP-induced inflammation is IL-1α- and IL-1β-dependent, as it was significantly inhibited by intra-peritoneal administration of both anakinra and anti-IL-1β antibodies. Accordingly, OCP-induced peritoneal inflammation was attenuated in IL-1α and IL-1β deficient mice. We investigated the contribution of the NALP3 inflammasome in OCP-induced inflammation. ASC-/- and NALP3-/- mice did not show any reduction of inflammation as assessed by neutrophil infiltration and MRP levels in peritoneal fluids, indicating that the OCP-induced inflammatory changes are independent of the classical NALP3 inflammasome in the mouse peritonitis model. Depletion of the resident macrophage population resulted in a significant decrease in crystal-induced neutrophil infiltration and proinflammatory cytokine production in vivo, whereas mast cell depletion had no effect.
Conclusion: These data indicate that macrophages, rather than mast cells, are important for initiating and driving OCP-induced inflammation. In addition, our results demonstrate that OCP induces a peritoneal inflammation that is dependent on both IL-1α and IL-1β, but does not require the NALP3 inflammasome.

Posters

P 1

Effectiveness of Rituximab versus alternative TNF antagonists in Preventing Radiographic Joint Damage in Rheumatoid Arthritis Patients with Inadequate Response to TNF antagonists

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Background: Observational studies have suggested that rheumatoid arthritis (RA) patients who experience an inadequate response to TNF antagonists (aTNF) may respond more favourably to a different class of biologic therapy, such as rituximab (RTX), than to an alternative aTNF. However, the relative effectiveness of these agents on long-term outcomes, such as radiographic damage, remains unclear.
Objective: To compare the effectiveness of RTX against aTNF agents in preventing joint damage progression in RA patients having experienced an inadequate response to at least one prior aTNF.
Methods: This is a prospective cohort study nested within SCQM-RA cohort including all patients with failure to at least one aTNF agent and subsequent treatment with either RTX or an alternative aTNF. Joint erosions (ERO) were assessed in 38 joints of hands and feet with a validated scoring method (Ratingen score, expressed in % of the maximum score) by a single reader, blinded to clinical history. The primary outcome of this analysis is the progression of ERO over time while on therapy. The evolution of ERO is analysed using regression models for longitudinal data, adjusting for potential confounders.

Results: 644 RA patients were included; 255 on RTX and 389 on an alternative aTNF (adalimumab 51%, etanercept 30%, infliximab 19%). Patients were followed over a median duration of 18 months and assessed on average with two sets of hand and feet X-rays. The two therapeutic groups were similar for most disease characteristics, but for some differences in disease duration, baseline DAS28 levels and number of previous aTNF failures. After adjusting for prognostic factors, we found no significant differences in the rates of ERO progression between patients on alternative aTNFs and RTX (p = 0.52). The ERO score progressed at an annual rate of +0.17% (95% CI: –0.18 + 0.52) in the aTNF group versus –0.01% (95% CI: –0.51 + 0.49) in the RTX group. Furthermore, we found no evidence for effect modification by rheumatoid factor or use of concomitant methotrexate. Longitudinal progression of functional disability (HAQ) produce qualitatively simlar results.
Conclusion: This observational study suggests that RTX is as effective as alternative aTNF in preventing radiographic joint damage in RA patients who have previously failed aTNF.

P 2

Efficacy of methotrexate in the management of chronic calcium pyrophosphate dihydrate (CPPD) arthropathy: an interim analysis of a randomized controlled trial

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Background: Calcium pyrophosphate dihydrate (CPPD) deposition may cause severe arthropathy and major joint destruction. There is currently no specific treatment to prevent CPPD deposition and the therapy of chronic or recurrent CPPD arthropathies can be problematic. We are conducting a randomized controlled trial (RCT) to test the efficacy of methotrexate (MTX) versus placebo (PBO) on symptoms and signs of chronic or recurrent CPPD arthropathy. We present here an interim analysis of the first 21 patients, which was performed by an external reviewer.
Objective: To assess the tolerance and efficacy of MTX in CPPD arthropathy and to validate the ethics and the rationale underlying this ongoing RCT.
Methods: This is a double-blind, crossover RCT, with a 2 month "wash-out" between the 3 month treatment periods. Patients with CPPD arthropathy are randomized to receive either weekly subcutaneous injections of 15 mg/week of MTX or similar injections of PBO. Inclusion criteria comprise definite CPPD deposition disease (McCarty diagnostic criteria), recurrent mono- or oligo-arthrits ("pseudogout") or persistent polyarthritis, and an insufficient response to NSAIDs, glucocorticoids or colchicine. Exclusion criteria are a positive rheumatoid factor or anti-CPP antibodies and contraindication to MTX therapy. Concomitant analgesic medication and additional glucocorticoids are allowed and number of pills assessed. The evaluation is performed in a double-blind manner at 0, 1, 2, 3 months and at 5, 6, 7, 8 months. The primary outcome is a reduction in arthritis pain level (VAS), and improvement in the DAS44 for polyarticular presentations or in number of flares for the pseudogout presentations. The analysis was performed on an intent-to-treat basis, using simple descriptive statistics, without significance testing.
Results: 21 patients from 5 centers were randomized and 16 patients completed all follow-up assessments. Baseline characteristics were balanced between the groups. During the study follow-up, 21 adverse events (AE) were reported, but no serious AE (hospitalization or permanent damage) occurred. Overall minor AE occurred more commonly on MTX (55% of patients) than on PBO (35% of patients). Patient's pain levels improved minimally in both groups (median VAS-pain decreased from 5 to 4.5 on MTX and from 6 to 5 on PBO). DAS44 levels did not vary substantially over time in either group (mean DAS44 decreased from 2.5 to 2.3 on MTX and from 2.7 to 2.2 on PBO). Forty percent of patients presented with pseudogout flares at baseline, after 3 months the proportion decreased to 17% in patients receiving MTX and to 24% in patients receiving PBO. A larger proportion of patients on MTX than on PBO was able to reduce analgesic or anti-inflammatory medications (40% versus 25%).
Conclusion: In this elderly population with chronic or recurrent CPPD arthropathy, minor AEs appear to be more frequent in patients receiving MTX than in those receiving PBO. In this interim analysis, no strong signal emerged in favour of MTX, warranting the continuation of the trial.

P 3

Clinical evaluation of chondroitin 4&6 sulfate (Condrosulf®) in the treatment of symptomatic hand osteoarthritis. A 6-month randomized double-blind, placebo controlled study

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Background: Symptomatic hand osteoarthritis (OA) is a common cause of consultation for both primary care physicians and in rheumatologists. Severe forms may lead to advanced structural changes, joint deformity and disability. Despite its frequency and severity there are currently only a limited number of therapeutic options.
Objective: To examine the effect of chondroitin 4&6 sulfate (CS) 800 mg daily on pain and function in patients with hand OA.
Patients and methods: This is an investigator initiated, randomized, placebo-controlled, single center, trial. Patients older than 40 years, with hand OA as defined by the ACR clinical and radiological criteria, suffering from regular joint pain (VAS ≥40/100 mm), and substantial functional impairement (functional index of hand OA (FIHAO): Dreiser score ≥6) were randomized to CS or placebo. Patients with other rheumatic conditions were excluded. The use of paracetamol, but not nonsteroidal anti-inflammatory drugs, was allowed during the study period. Primary end points included global spontaneous pain (VAS) and functional impairment (FIHOA). Secondary endpoints included global improvement (VAS_improvement), grip strength, duration of morning stiffness, consumption of paracetamol, and drug safety. Both the data transcription and the statistical analysis were replicated by the investigators, independently from the pharmaceutical study sponsor.
Results: 163 patients were randomized, 81 in the CS and 82 in the placebo groups. One patient in the CS group was excluded from the ITT analysis for protocol violation. Demographic data including age, sex, BMI, blood pressure were perfectly matched in the two groups. Mean ± SD global pain VAS and Dreiser scores in the CS and placebo groups were 54.9 ± 14.2 and 11.0 ± 4.1 and 53.6 ± 14.2 and 10.3 ± 3.8, respectively. Other clinical characteristics including grip strength, number of days of painful flares, duration of morning stiffness were also balanced between the two groups. At six months, the improvement of global pain (VAS) and FIHOA were significantly more important in the CS group (–20 ± 26.6 mm and –2.9 ± 5.3) than in the placebo group (–11.3 ± 24.0 and –0.7 ± 4.8, significance P = 0.03 and P = 0.008, respectively). The evaluation of global improvement (VAS_improvement) was also significantly better in the CS group (P = 0.04), whereas grip strength and duration of morning stiffness were not significantly different. There was also no difference regarding the frequency of adverse events.
Conclusion: CS 800 mg daily is effective and safe in the treatment of symptomatic hand OA.

P 4

Increased MHCII expression in the synovium during collagen induced arthritis is driven by the promoter I of CIITA in macrophages

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Introduction: Rheumatoid fibroblast-like synoviocytes (FLS) express MHC class II (MHCII) molecules and function as antigen-presenting cells (APC) in vitro. We tested the contribution of ectopic MHCII expression on FLS during experimental arthritis in mice rendered specifically deficient for MHCII expression on FLS and mesenchymal cells.
Methods: pIV-/- mice are deficient in MCHII expression on FLS. They are also resistant to T cell mediated autoimmunity since they lack positive selection of CD4+ T cells. To evaluate the role of the lack of peripheral MHCII expression by FLS in collagen induced arthritis (CIA), we reconstituted the CD4+ T cell repertoire by introducing a thymic specific transgene (CIITA-K14) in the DBA/1 background. CIA was induced by immunization with bovine type 2 collagen (CII) in complete Freund's adjuvant (day 1), followed by a boost of CII in PBS i.p. at day 22, in pIV-/- knockout mice, pIV-/- CIITA-K14 transgenic mice and control littermates. MHCII and CIITA isoforms were quantified by RT-qPCR in arthritic paws at sacrifice (day 43). MHCII protein expression was assessed by flow cytometry (FACS) on mouse FLS and by immunohistochemistry on frozen arthritic knee sections.
Results: In vitro, MHCII induction was completely absent in pIV-/- FLS while synovial macrophages express normal levels of MHCII via the CIITA pI isoform. The CIITA-K14 transgene reconstituted normal CD4+ T cell numbers in pIV-/- mice. After immunization, immune responses towards CII and arthritis incidence were similar in pIV-/- CIITA-K14 compared to control littermates. pIV-/- mice were fully protected due to their lack of CD4+ T cells. The arthritis scores of pIV-/- CIITA-K14 transgenic were slightly, but not significantly, lower than those of control littermates. By co-immunhistochemistry for F4/80 and MHCII,

macrophages were the main source of MHCII expressing cells in arthritic knees in all groups of mice.
Conclusion: Deletion of the inducible isoform pIV of CIITA in the periphery did not significantly decrease immune responses and arthritis severity in the CIA model. Local expression of MHCII and CIITA pI isoform mRNA levels were significantly increased during arthritis, highlighting the dominant role of MHCII positive macrophages.

P 5

Tocilizumab in a Patient with Ankylosing Spondylitis and Crohn's Disease Refractory to TNF Antagonists

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Introduction: Tumor necrosis factor inhibitors (anti-TNF) have dramatically improved the management of ankylosing spondylitis (AS). However, up to 20% of patients have an inadequate response to anti-TNF therapy due to inefficacy or adverse events [1]. No biological agent with a target other than TNF has so far demonstrated efficacy for AS patients.
Case report: We present the case of a 30-year old man with a history of severe HLA-B27 positive AS and Crohn's disease (CD) for over 14 years, recurrent uveitis and psoriasis. He demonstrated secondary failure to 3 anti-TNF agents: infliximab, adalimumab and certozilumab and did not experience any improvement following treatment with abatacept. He ultimately demonstrated a good and sustained clinical (swollen joint count and BASDAI) and biological response (normalisation of the acute-phase response) to tocilizumab, an antibody against interleukin (IL)-6 receptor. We did not observe any adverse event after a follow-up of 10 months.
Discussion: This case provides the opportunity to review the data on the role of IL-6 in AS and to discuss the potential use of IL-6 targeting agents in the treatment of spondylarthropathies. A randomised controlled trial suggested efficacy of fortnightly 8 mg/kg infusions of tocilizumab in patients with CD [2] and a recent case report also described successful treatment of reactive arthritis with tocilizumab [3]. This is the first case report of successful therapy with tocilizumab in AS. It emphasizes the importance of investigating other biological targets in AS and suggests that IL-6 targeting warrants further research in this disease.
References: 1 Braun J, et al. Curr Opin Rheumatol. 2009;21:324–34. 2 Ito H, et al. Gastroenterology. 2004;126(4):989–96. 3 Tanaka T, et al. Arthritis Rheum. 2009;61(12):1762–4.

P 6

Work Related Characteristics of Back and Neck Pain among Employees of a Swiss University Hospital

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Study design: Mailed survey.
Objectives: To define the prevalence of spinal pain among employees of a large teaching hospital and to identify risk factors for spinal pain and its consequences.
Background: Back and neck pain (spinal pain) is a significant source of disability and distress for individuals and has major economic consequences for society. The causes of spinal pain are complex and not fully understood. In particular, little is known about the importance of work categories and work characteristics for the prevalence and consequences of spinal pain.
Methods: A mailed survey was carried out in a random sample of 2700 employees stratified for occupational categories (administration staff, nurses, nurse assistants, physicians, support staff and allied health professionals). The questionnaire measured self-reported spinal pain, consequences of pain, and work characteristics
Results: The response rate was 48.1% (1298/2700). The one-year prevalence of spinal pain was 67.3%, highest among nurses (75.6%) and lowest among support staff (54.9%). Reported work characteristics associated with spinal pain included frequent work at a poorly adapted work station (odds ratio (OR) 1.90 [1.24–2.93]) and having to maintain a position for a long time (OR 1.71 [1.25–2.34]). No significant correlations were observed with lifting, patient handling, material handling, or working on nightshift. Sickness leave due to spinal pain was significantly associated with duration of pain episode (OR 4.08 for >3 months compared to less than 10 days), and with work categories (OR 2.58 for nurse assistants compared to nurses).
Conclusion: In this population of hospital employees, being a nurse, working at a poorly adapted work place, and having to maintain positions for a long time were related independently to spinal pain. Nurse assistants had a higher risk of work absenteeism.

P 7

Decrease in apprehension after multidisciplinary treatment in chronic low back pain patients

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Chronic low back pain (CLBP) is a expensive according to direct and indirect costs. The most expensive patients are those who are on long sick leave.There are different treatment possibilities, but surgery is not superior to conservative treatment. But which part in a multidisciplinary treatment program is important to have a successful result? The aim of this study was to look on the different parts of our multidisciplinary program, to find out the important components.
Methods: We have studied the results of our 400 patients during one year after a multidisciplinary treatment program. The program contained physical education, occupational activities and psychological – cognitive- participation. We measured the abdominal muscle forces (Shirado), the lumbar muscles (Biering-Sörensen), and the cardiac endurance (Bruce test) in association with different pain scales (Oswestry; Roland–Morris, Dallas pain scale; SF-36 and HADS).
Results: There was a clear increase in muscle force after 3 weeks intensive training (Shirado and Biering-Sörensen) but it didn't sustain over the year. The global endurance increase seen with the Bruce was maintained for a year. There was a decrease of pain, more clearly seen in the psychological scores: pain behaviour and apprehension. The work capacity wasn't associated with the physical increase, but with the evolution on the psychological plan.
Conclusion: So even though the physical evolution didn't change, there was a global positive effect, with a back to work of 67% of de patients. It was correlated with a decrease in psychological parts of the different pain questioners. We can therefore conclude that the important part in these global functional restoration programs is the increase in confidence both directly and indirectly and it has to be reinforced. Even then that the patients see an increase of physical parameters in the beginning, will reinforce there conviction to continue.

P 8

A Single High Dose of Oral Vitamin D3 Is Not Enough to Correct Insufficiency and Deficiency in a Rheumatologic Population

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Introduction: Vitamin D plays a major role in bone metabolism and neuromuscular function. Supplementation with vitamin D is effective to reduce the risk of fall and of fracture. However adherence to oral daily vitamin D supplementation is low. Screening and correcting vitamin D insufficiency in a general rheumatologic population could improve both morbidity and quality of life in these patients with chronic painful disorders and at high risk of osteoporosis. After determining the prevalence of vitamin D deficiency in this population, we evaluated if supplementation with a single high dose of oral 25-OH vitamin D3 was sufficient to correct this abnormality.
Methods: During one month (November 2009), levels of 25-OH vitamin D were systematically determined in our rheumatology outpatient clinic and classified into three groups: vitamin D deficiency (<10 µg/l), vitamin D insufficiency (10 to 30 µg/l) or normal vitamin D (>30 µg/l). Patients with insufficiency or deficiency received respectively a single high dose of 300000 IU or 600000 IU oral vitamin D3. In addition, all patients with osteoporosis were prescribed daily supplement of calcium (1 g) and vitamin D (800 IU). 25-OH vitamin D levels were reevaluated after 3 months.

	Time 0 month			Time 3 months			
	Mean vit D (µg/l)	Deficiency	Insufficiency	Mean vit D (µg/l)	Deficiency	Insufficiency	Normal
All (N=173)	18.8 (1.5-29.6)	8%	92%	29.8 (7.1-85.2)	1.7%	50.3%	48%
+CaD3 (N=62, 36%)	21.6 (8.3-29-6)	5%	95%	32.4 (13.2-85.2)	0%	42%	58%
No CaD3 (N=111, 64%)	17.3 (1.5-29.1)	10%	90%	28.4 (7.1-55.5)	3%	55%	42%
IRD (N=139)	18.6 (4.3-29.2)	9%	91%	29.4 (7.1-49.8)	2%	50%	48%
+ CaD3 (N=48, 35%)	20.9 (8.3-29.2)	6%	94%	31.5 (13.2-47.9)	0%	44%	56%
No CaD3 (N=91, 65%)	17.3 (4.3-29.1)	11%	89%	28.2 (7.1-49.8)	3%	53%	44%
OP (N=25)	19.8 (1.5-29.6)	8%	92%	34.2 (12.8-85.2)	0%	40%	60%
+ CaD3 (N=19, 76%)	22.0 (9.3-29.6)	5%	95%	35.2 (19.8-85.2)	0%	37%	63%
No CaD3 (N=6, 24%)	13.0 (1.5-26.7)	17%	83%	30.7 (12.8-49.8)	0%	50%	50%
DD (N=20)	19.4 (12.1-29.1)	0%	100%	28.9 (21.2-55.5)	0%	65%	35%
+ CaD3 (N=2, 10%)	26.1 (24.4-27.8)	0%	100%	31.5 (31.5)	0%	0%	100%
No CaD3 (N=18, 90%)	18.6 (12.1-29.1)	0%	100%	28.6 (21.2-55.5)	0%	72%	28%

Results: Vitamin D levels were initially determined in 292 patients (mean age 53, 211 women, 87% Caucasian). 77% had inflammatory rheumatologic disease (IRD), 20% osteoporosis (OP) and 12% degenerative disease (DD). Vitamin D deficiency was present in 20 (6.8%), while 225 (77.1%) had insufficiency. Of the 245 patients with levels <30 µg/l, a new determination of vitamin D level was available in 173 (71%) at 3 months.
Conclusion: Vitamin D insufficiency is highly prevalent in our rheumatologic population (84%), and is not adequately corrected by a single high dose of oral vitamin D3 in more than half of the patients with IRD and DD. In patients with OP, despite association of a single high dose with daily oral vitamin D supplementation, 40% of patients are still deficient when reevaluated at 3 months.

P 9

IVA in addition to BMD can change the osteoporosis management in 25% of clinical routine patients

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Introduction: Vertebral fracture is one of the major osteoporotic fractures which are unfortunately very often undetected. In addition, it is well known that prevalent vertebral fracture increases dramatically the risk of future additional fracture. Instant Vertebral Assessment (IVA) has been introduced in DXA device couple years ago to ease the detection of such fracture when routine DXA are performed. To correctly use such tool, ISCD provided clinical recommendation on when and how to use it. The aim of our study was to evaluate the ISCD guidelines in clinical routine patients and see how often it may change of patient management.
Methods: During two months (March and April 2010), a medical questionnaire was systematically given to our clinical routine patient to check the validity of ISCD IVA recommendations in our population. In addition, all women had BMD measurement at AP spine, Femur and 1/3 radius using a Discovery A System (Hologic, Waltham, USA). When appropriate, IVA measurement had been performed on the same DXA system and had been centrally evaluated by two trained Doctors for fracture status according to the semi-quantitative method of Genant. The reading had been performed when possible between L5 and T4.
Results: Out of 210 women seen in the consultation, 109 (52%) of them (mean age 68.2 ± 11.5 years) fulfilled the necessary criteria to have an IVA measurement. Out of these 109 women, 43 (incidence 39.4%) had osteoporosis at one of the three skeletal sites and 31 (incidence 28.4%) had at least one vertebral fracture. 14.7% of women had both osteoporosis and at least one vertebral fracture classifying them as “severe osteoporosis” while 46.8% did not have osteoporosis nor vertebral fracture. 24.8% of the women had osteoporosis but no vertebral fracture while 13.8% of women did have osteoporosis and vertebral fracture (clinical osteoporosis).
Conclusion: In conclusion, in 52% of our patients, IVA was needed according to ISCD criteria. In half of them the IVA test influenced of patient management either by changing the type of treatment of simply by classifying patient as “clinical osteoporosis”. IVA appears to be an important tool in clinical routine but unfortunately is not yet very often used in most of the centers.

P 10

Instant Vertebral Assessment as a tool in ankylosing spondylitis assessment: a pilot study

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Introduction: While it is known that there is a high prevalence of vertebral fractures in ankylosing spondylitis (AS) patients, most modern assessment of structural damage focuses solely on ankylosis. Instant vertebral fracture assessment (IVA) is a technique that gives morphometric images of the spine at the time of BMD measurement using dual X-ray absorptiometry (DXA). We performed a pilot study to compare IVA to conventional X-ray imaging at detecting syndesmophytes, with the potential added benefits of BMD measurements.
Methods: 20 consecutive male AS patients fulfilling the modified AS New York classification criteria followed at our outpatient clinic and with at least one syndesmophyte on a recent lumbar or cervical lateral spine films were recruited. Each patient underwent a DXA with measurement of BMD, coupled to a single-energy 20 s morphometry scans (IVA) using the Hologic Delphi bone densitometer in lateral position. Data on additional clinical risk factors for osteoporosis were collected. Lateral spine radiographs (cervical and lumbar) were scored independently by two readers using the published mSSAS scoring system from 0 to 3. IVA images were scored similarly using an adaptation of this scoring system from 0 to 3 where erosions (score of 1) were not recorded. Agreement between observers for the presence of syndesmophytes on X-ray and IVA was assessed using kappa statistics. Standard WHO T-score was used for osteoporosis and osteopenia definition.
Results: 19 patients underwent the planned DXA and IVA examinations. Mean disease duration was 15 years (2 to 40) and mean age of 52.4 years (27–73). Six (32%) were HLA-B27 positive, 4 (21%) had concomitant inflammatory bowel disease and 16 (85%) were currently on anti-TNF therapy. All patients had at least one syndesmophyte identified on standard lateral spine films, with 2 patients (10.5%) presenting a complete ankylosing of the spine, 3 (15.8%) syndesmophytes only on the cervical spine, and one only on the lumbar area. For conventional X-ray, the intra-reader reproducibility was 94.3% (kappa test 83.5%, IC 95%: 0.7–0.97), while the inter-reader agreement was 98.6% (kappa test 96% IC 95%: 0.82-1.09). For IVA, the reproducibility was similar with 92.8% for intra-reader (kappa test 79.9% IC 95%: 0.66–0.93), and 93.8% for inter-reader (kappa test 82.8% IC 95%: 0.69–0.96). The agreement between the two techniques was excellent (90.4%) (kappa test 73.4% IC 95% : 0.6–0.86). Out of 19 patients included in the study, DXA measurement allows the identification of ten patients (52%) with osteopenia as well as two with osteoporosis. However out of the two osteoporotic patients, one already had previous diagnosis of osteoporosis and was treated with alendronate, while the second one reported a low-energy fracture of vertebral fracture and thus was also already diagnosed as clinical osteoporosis. In the osteopenic patients, the median duration of the disease was 12.3 years, and only two of them had known history suggestive of malabsorption related to bowel involvement.
Conclusion: This pilot study demonstrates the potential of IVA to assess structural damage in AS patients. It allows visualization of syndesmophytes with a much lower ionizing radiation and adds the benefit of BMD measurement with potential major impact of long term quality of life in this population.

P 11

A screening strategy for rheumatoid arthritis in first degree relatives of patients with RA

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Introduction: During the preclinical phase of RA, auto-antibodies are often already present and synovitis can be demonstrated on histology in clinically uninflamed joints. Biomarkers and clinical risk factors of pre-symptomatic disease exist and suggest that screening at risk populations for early detection of RA and treatment are not out of the realm of the possible. The aim of this study is to develop and evaluate a screening strategy for the development of RA in first degree relatives (FDRs) of patients with RA.
Objective: To examine the clinical characteristics of FDRs of RA patients enrolled in a screening study.
Methods: Descriptive analysis of the clinical characteristics of a cohort of FDRs of patients with RA.
Results: We started to assemble a cohort of FDRs of RA patients in all academic rheumatology clinics of Switzerland (see author affiliations above). After the few months of recruitement (average of 7 months), 72 FDRs of RA patients have been enrolled. On average, participants have 1.3 diseased family members, which is generally a parent (83%) and only in 17% a diseased sibling. Participants are relatively young (mean 39 years), which tends to be approximatively the same age at which their diseased family member developed RA (mean 41 years). Participants are mostly female (67%), without significant comorbidities, and with normal weight (mean BMI 23.7). Surprisingly, many participants presented several tender joints (med 5, IQR: 3–8) on examination at inclusion, but only one had swollen joints (2*).
Conclusion: FDR participants in the screening study tend to enrol because of concerns of developing RA, which may explain a relatively high number of tender joints on examination and an inclusion age associated with the age of disease onset of the diseased relative.

P 12

Behcet’s disease: Successful treatment with Infliximab in 8 patients with severe vascular manifestations

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Introduction: Vascular inflammatory lesions of arteries and veins in Behcet`s disease (BD) are rare but may be life-threatening. Standard therapeutic concepts do not exist. We report 8 patients with severe vasculitic BD lesions treated with infliximab as acute management combined with basic immunosuppression.
Patients and therapy: Eight patients (5 male, 3 female, age at diagnosis 23–42 years) with clinical evidence of BD. Two had an aortic involvement with one of them undergoing emergency aortic valve

replacement twice, 1 presented with hemoptysis due to pulmonary aneurysm, 1 with recurrent venous thrombosis of the pelvic veins, 1 suffered both venous and arterial thromboses of his thigh and three showed retinal vasculitis, one of them suffering from concomittant cerebral vasculitis. Infliximab was initiated during acute vasculitis with a mean dosage of 3–5 mg/kg bodyweight either as first line therapy in 3 patients or as add-on after failure of conventional immunosuppression in 4 and failure of cyclophosphamide in 1 patient. Infliximab could be stopped in 3 patients, dosage intervals could be extended to a maximum of 8 weeks in 5 patients. Conventional immunosuppression was begun or continued with either methotrexate (10–20 mg/week s.c.), cyclosporine (3 mg/kg bodyweight) or azathioprine (1–2 mg/kg bodyweight) and combined with tapering dosages of glucocorticoids. Warfarin was maintained in 4/8 patients.
Results: Reduction of inflammatory signs and symptoms was recognized within 2–5 days after initiation of infliximab in all patients without recurrent or additional vascular complications. Visual acuity increased in patients with retinal vasculitis. Vascular grafts remained patent. Infliximab as well as basic immunosuppression was well tolerated without major side-effects.
Conclusion: Infliximab is effective in reducing inflammatory vasculitic activity in BD (either as first-line or add-on therapy) in patients with severe vascular involvement. We recommend infliximab as short-course first-line therapy in vascular BD at a dose of 5 mg/kg body weight. Basic immunosuppression should be initiated and/or continued as long-term therapy.
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P 13

ANCA positive vasculitis: misleading digital ischemia and successful fortified immunosuppressive treatment

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Introduction: ANCA-positive vasculitis may present with digital ischemia and infarction. We report the case of a patient with prolonged peripheral ischemia leading to the loss of 7 finger tips.
Patient and therapy: A 59-years old man presented with a 3-week history of fever, malaise, epistaxis and finally spotted, progressive cyanotic lesions on 7/10 finger tips. Endocarditis and other infectious foci were ruled out. Vasculitis work-up showed high titres of PR3-positive c-ANCAs. Nasal biopsy revealed acute vasculitic lesions in small-size arteries. In MRI small cerebellar ischemic lesions were detected. Furthermore, microhematuria, microalbuminuria, ECG-abnormalities with R-reduction in antero-septal and inferior leads were found. Collectively the findings proved to be caused by an ANCA-associated vasculitis, probably a generalized Wegener's disease. Immunosuppression was initiated with solumedrol pulses, plasmapheresis and i.v. cyclophosphamide.
Conclusion: This case illustrates the need for a rapid work-up if vasculitis is suspected. At the time of diagnosis infarcts of the end phalanges of 7 fingers were already established. In contrast, all other disease manifestations were easily controlled by adapted immunosuppression.

P 14

Utility of ultrasound guided infiltrations in the painful shoulders: a randomized study of 70 cases

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Background: infiltration of painful shoulders with local steroid induces significant improvement in many cases. Ultrasound allows a more precise diagnosis of the causes of pain than clinical evaluation and therefore could be an interesting way of predicting the response to the steroid infiltration.
Objectives: were double: first, to see whether sonographic guided infiltration oriented according to the echographic diagnosis resulted in a better outcome of pain and function than blind subacromial infiltrations, secondly to evaluate whether a precise sonographic diagnosis has any impact on the result of the infiltration.
Methods: 70 consecutive patients were studied. All the patients had a complete clinical and sonographic evaluation at day 0 and at 6 weeks. Patients were randomized to receive either a blind sub-acromial infiltration of bethamethasone 7 mg independently of the ultrasound diagnosis or sonographic guided injection oriented according to ultrasound diagnosis. The follow-up clinical evaluations were performed blind to the results of initial sonographic and clinical assessments by another rheumatologist than the one who performed the infiltration. Pain by a vocal numerical rating scale (range from 0 to 10) and function by standardized modified Constant score were assessed at day 0, 2, 6 and 12 weeks.
Results: 67 completed the study (35 blind, 32 ultrasound). The two groups were comparable for gender, age, pain intensity at baseline, duration of pain before the infiltration and for most of the echographic diagnosis. Ultrasound- guided infiltration resulted in a better improvement of pain and function but only night pain was signicantly reduced at 2 and 6 weeks in the ultrasound infiltrated compared the blind infiltrated patients. The same was found in the patients with calcification and bursitis infiltrated under ultrasound. Ultrasound diagnosis has no impact on: initial degree diurnal pain, maximum and significant pain improvement at 2 weeks, progressive reoccurrence of pain at 6 and 12 weeks, improvement in Constant score at 6 weeks and change in ultrasound image at 6 weeks. Initial night pain was significantly higher in the complete cuff rupture patients than in the capsulite patients. Pain reduction was maximal and significant reduced at 2, 6 and 12 weeks in comparison to all other groups when calcification was present. Capsulite was associated with poorer initial and final Constant score and a higher pain score at 12 weeks also found in the complete cuff rupture group.
Conclusion: Infitration of painful shoulder under sonograhic guidance according to the diagnostic image add significant benefit to night pain reduction at 2 and 6 weeks. Some particular ultrasound diagnosis have an impact on the pain response especially night pain although infiltration reduces significantly the pain whatever the initial ultrasound diagnosis.

P 15

Improvements after interdisciplinary rehabilitation of whiplash injury

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Background: In Switzerland, 10000 car accidents lead to whiplash injuries with annual cost of over 500 Billion CHF. The aim of this study was to examine state and change of bio-psychosocial health and quality of life of patients after whiplash injury, before and after an inpatient interdisciplinary pain management program.
Methods: Observational, prospective cohort study (n = 103) using medical record data and standardized self-assessments to determine effects by means of standardized effect sizes (ES). ES ≥0.50 reflect moderate, ES ≥0.80 high effects. The four-week inpatient therapy program consisted of drug adaptation, graded activity exercise, relaxation therapies, and behavioral therapy (>100 h of therapy).
Results: After rehabilitation, pain improved by ES up to 0.65, function/role performance up to 0.87, vitality up to 0.67, coping ("catastrophizing") up to 0.41 and depression up to 0.45. At the 6 month follow-up, these effects remained with ES between 0.45 and 0.87. The median working capacity improved from 8 hours per week at baseline to 21 hours on the follow-ups. These effects were observed in severely affected patients with poor response to previous outpatient therapies.
Conclusion: The rehabilitation program was associated with moderate to large midterm improvements in important health dimensions, medication reduction and working capacity.

P 16

Costs related to treatment with TNF alpha inhibiting agents in Switzerland

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Introduction: The reasons for rising health care costs are one of the most prominent areas of interest in the analysis of health care structures. Aim of this study was to obtain detailed data not only on costs but also treatment patterns in the utilization of TNF-alpha inhibiting agents in patients treated by Swiss rheumatologists.
Methods: Insurance claims data from 1,433 individuals were identified and extracted for the years 2005-08 from the database of the Helsana insurance. Research questions address not only annualized costs in different domains but also treatments patterns (e.g., adherence, dosing). Specific areas of interest were: drug costs/year, additional healthcare costs/year, costs separated by disease areas, costs in relation to dosing and adherence, continuity of care with respect to individual compounds, as well as the identification of specific patient clusters. Data of various different subgroups which were defined with respect to the different approved indications (e.g., rheumatology, gastroenterology) were analyzed using descriptive as well as explorative statistics and are presented in detailed overviews. The focus was set on rheumatologic patients.
Results: Patients treated by rheumatologists required a substantial resource use ranging from about 20000–27000 CHF annually depending on the underlying drug therapy and subgroup

segmentation. In addition, a few general trends could be observed: a) annual overall direct costs for i.v. therapy (infliximab) were higher in comparison to the available s.c. treatment options (adalimumab and etanercept); b) annual i.v. related ambulatory hospital costs were higher as with the s.c. options; c) annual i.v. related laboratory costs tended also to be higher than under therapy with any s.c. option; d) etanercept and adalimumab were comparable with respect to overall costs consistently throughout the analyses. The results were coherent across almost all study segments.
Conclusion: In a situation with various available and also effective treatment options information on relative costs between the different options are of interest. Further studies, including about the combination of costs with outcome parameters are needed.
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P 17

Brain abscess in immunosuppressed patients – not always infection

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Introduction: Clinical features of brain abscesses are extremely variable and nonspecific. Symptoms vary from signs of increased intracranial pressure, focal neurologic abnormalities to fever of unknown origin. A high alertness is needed as early detection is crucial for the outcome. We report two cases of cerebral abscesses of different etiology in immunosuppressed patients.
Report of cases: Case 1: A 64-years old woman, known for seronegative polyarthritis and treated with abatacept, presented because of diplopia. Magnetic resonance imaging (MRI) revealed destructed walls of sinus maxillares, orbita and lamina papyracea with penetration of the dura mater and localized intracranial inflammatory process. Endoscopic (transnasal) biopsy showed a chronic inflammation with plenty of staphylococcus aureus, however, without characteristic findings of Wegener's disease (WG) or NKT cell lymphoma. Immunosuppressive therapy was stopped and antibiotic treatment was begun.
Case 2: A 62-years old woman with known Wegener's granulomatosis treated with Methotrexat and glucocorticoids presented because of severe headache and intermittent situative disorientation. MRI revealed intracranial frontobasal lesions with a high suspicion of infectious abscesses. The patient underwent craniotomy and biopsy of several lesions. Sterile granulomata as a manifestation of the WG. The patient received high-dose glucocorticoids and immunosuppressive therapy was intensified with infliximab and cyclophosphamid.
Discussion: Cerebral involvement of localized Wegener's granulomatosis is rare. It may develop subclinically with the risk of diagnosis delay. MR and CT provide important information but immuno-histology and microbial analysis are needed for the definitive diagnosis and to rule out an infectious or neoplastic cause. Destruction of paranasal sinuses predisposes for intracranial bacterial spread.

P 18

The influence of immunosuppressive therapy and underlying diseases on vaccine responses to influenza A H1N1/09 vaccines in inflammatory rheumatic diseases

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Background: Influenza A H1N1 is a new virus that emerged in spring 2009 and rapidly spread around the world causing a pandemic. As patients with inflammatory rheumatic diseases (IRD) exhibit some form of immunodeficiency related to their diseases and the use of immunosuppressive drugs, the Swiss Society of Rheumatology recommended the vaccination of all IRD patients under immuno-suppressive agents. However, two important questions remain unresolved: 1) are immunocompromised hosts able to raise successful vaccine responses, 2) is the use of adjuvanted vaccines safe in patients with autoimmune diseases.
Objectives: To determine the efficacy and safety of influenza A H1N1/09 vaccine formulated in a lipid adjuvant (squalene) in patients with IRD.
Patients and methods: 173 patients with IRD and 138 healthy controls were included from November 2009 to January 2010 in this prospective, open-labeled, single center, parallel-cohorts study. Among IRD patients, there were 82 cases of rheumatoid arthritis (RA), 45 cases of spondylarthropathies (SpA), and 46 cases of connective tissue diseases (18 systemic lupus erythematosus (SLE)) or vasculitis. All received a first vaccine dose and 154 (89%), the second prescheduled vaccine dose. Safety after vaccination was assessed, respectively, in 173 and 149 patients using medical history and clinical indices of disease activity (DAS28, RADAI, and HAQ for RA, BASDAI for axial SpA, SLEDAI for SLE, and BVAS for vasculitis). The kinetic of the vaccine response and antibody titers (using a standardized in-house hemagglutination inhibition assay) were assessed after the first and the second dose and compared to titers obtained in a control group of healthy individuals vaccinated once. Cellular immune responses to influenza H1N1/09 vaccine will be also determined in a subset of patients and controls.
Results: Disease modifying antirheumatic drugs were used in 85% of RA, 63% of SpA, 94% of SLE patients; oral corticosteroids in 31% of RA, 11% of SpA, and 70 of SLE patients; anti-TNF in 43% of RA and 71% of SpA; and rituximab in 21% of RA and 11% of SLE patients. The different indices of disease activity were not significantly different at baseline and after vaccination. Despite immunosuppression, injection-site tolerability and systemic inflammatory reactions were similar in patients with IRD than in healthy controls. The analysis of the kinetic and the pattern of vaccine immune responses in the different IRD patient groups in comparison with those of healthy subjects is in progress and will be presented.
Conclusions: The adjuvanted vaccine against influenza A H1N1/09 is well tolerated and does not induce short-term exacerbation in patients with IRD treated with immunosuppressive agents.

P 19

Identification of genetic markers of rheumatoid arthritis severity

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Introduction: Recent genome wide and candidate gene association studies have identified over 20 confirmed single nucleotide polymorphisms (SNPs) predisposing to rheumatoid arthritis RA (susceptibility loci). However, the genetic variants identified so far do not predict clinical outcomes such as erosions, disability or response to treatment. We therefore sought to identify genetic markers of outcome, primarily of disease severity, in patients with recent-onset inflammatory polyarthritis (IP).
Methods: The Norfolk arthritis register (NOAR) is a primary care-based inception cohort of subjects with IP recruited at symptom onset and followed prospectively. Demographic and clinical data are recorded at inclusion and at yearly assessments thereafter. Anti citrullinated peptide antibody status (ACPAs) is determined at study entry. A subset of 372 patients has been genotyped for 370,404 single nucleotide polymorphisms (SNPs) by genome-wide arrays (Illumina). The association of SNP markers with clinical and radiological markers of disease severity was investigated using the presence of erosions by 5 years as the primary outcome measure. Adjustment for the presence of ACPA, a known marker of disease severity, and for receiving disease modifying anti-rheumatic medications was incorporated into the analysis.
Results: The baseline characteristics of the 372 genotyped patients of the NOAR cohorts show that 84% of the patients satisfied ACR criteria for RA; 62% carried at least one copy of an HLA-DRB1 allele and 48% were erosive by 5 years. Preliminary results on genome-wide association studies revealed a number of SNPs with evidence for association with erosions by year 5 of follow-up.
Discussion: We have found a number of SNPs with strong evidence for association with the presence of erosions by 5 years. The identification of genetic predictors of severity at presentation could be used to predict which patients are likely to develop erosive disease, and it may be possible to target these patients for more aggressive treatment earlier in their disease course. If replicated, these genetic markers may improve the predictive value of ACPA in identifying patients likely to experience a severe disease course and pave the way for a more personalised approach to medicine.

P 20

T cell co-stimulation blockade prevents tumour necrosis factor inhibitor induced palmoplantar pustulosis

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We are reporting on a case of palmoplantar pustulosis (PPP), which is a known side effect of the tumour necrosis factor (TNF) blocking agents. After failing to respond to standard care, the asymmetric HLAB27 positive oligoarthritis went into remission by using Etanercept. PPP started 6 months after introduction of Etanercept and persisted despite discontinuing the TNF blocker and administering topical corticosteroids. PPP improved upon recombinant CTLA4-Ig (Abatacept), but the inflammation of the joints did not reduce. Under prophylactic continuation of CTLA4-Ig it was possible to subsequently

re-expose the patient to Etanercept, this time without PPP exacerbation. This led to a new complete remission of the exacerbated arthritis for more than a year. The observation strongly suggests that there are different immunological pathways for the arthritis and PPP in the same individual. Furthermore we suspect that the T-cells are involved in the causal relationship between the TNF blockade and PPP. We did not notice a high infection frequency under the combined therapy. Although not the first treatment option, two biologics can be applied simultaneously after careful consideration of the potential interactions, higher infection rate and cost.

P 21

Efficacy of canakinumab (ACZ885) compared to triamcinolone acetonide for treatment of acute flares and prevention of recurrent flares in gouty arthritis patients

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Aim: This study determined the target dose of canakinumab (a fully human anti-IL-1β monoclonal antibody) for treatment of acute flares in gouty arthritis patients.
Methods: In this 8-week, dose-ranging, multicenter, blinded, double-dummy, active-controlled trial, patients (aged ≥18–≤80 years) with an acute gout flare, refractory to or contraindicated to NSAIDs and/or colchicine were randomized to one subcutaneous dose of canakinumab (10, 25, 50, 90, or 150 mg) or one intra muscular dose of triamcinolone acetonide (TA) [40 mg]. The primary variable was assessed 72 hours post-dose, measured on a 0–100 mm VAS pain scale.
Results: 200 patients were randomized (canakinumab n = 143, TA n = 57), and 191 completed the study. Canakinumab showed a statistically significant dose response for pain (VAS) at 72 hours. Canakinumab 150 mg showed superior pain relief compared to TA starting from 24 hours: estimated mean difference in pain intensity on 0–100 mm VAS was –11.5 at 24 hours, –18.2 at 48 hours, and –19.2 at 72 hours (all p <0.05). Canakinumab 150 mg provided a rapid onset of pain relief: median time to 50% reduction in pain was reached at one day with canakinumab 150 mg vs. two days for TA (p = 0.0006). At Week 8, recurrent flares occurred in one patient (3.7%) on canakinumab 150 mg vs 25 (44.6%) patients on TA (relative risk reduction 94%, p = 0.006). Median CRP/SAA levels were normalized by Day 7 with all canakinumab doses above 10 mg and remained below the Upper Limit of Normal [(ULN): CRP 3.0 mg/L; SAA 6.7 mg/L)] for rest of the study in contrast to the TA group, where the median CRP levels remained above the ULN throughout the study while median SAA levels decreased below ULN 28 days after first treatment. Serious adverse events (canakinumab n = 4, TA n = 1) were not considered to be treatment-related by investigators. No discontinuations occurred due to adverse events.
Conclusions: Canakinumab 150 mg provided faster onset and superior pain relief compared to TA for acute flares in gouty arthritis patients refractory to or contraindicated to standard treatments. CRP/SAA levels were normalized by Day 7 with all doses of canakinumab above 10 mg, while levels did not normalize in the TA group. Canakinumab 150 mg prevented recurrence of gout flares with a relative risk reduction compared to TA of 94% 8 weeks post-dose, and was well tolerated.

P 22

The humeroradial impingement

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Lateral pain of the elbow is frequently reported. Impingement of the humeroradial fold or a synovial fringe is a seldom evoked cause, sometimes ignored. Nonetheless, this etiology should be remembered, especially in young adults performing sport activities and in heavy workers. This presentation reports on a young lady, born in 1990 who came to the outpatient clinic for a progressive limitation of her left elbow which started one year before. She experienced a few local inflammatory episodes, especially after horse riding. There was no synovitis on clinical examination but pressure on the humeroradial joint space was painful. There was also a lack of 15° joint extension. Full supination and pronation against resistance when the arm was completely stretched recalled the spontaneous pain. Radiographs were normal. Conventional ultrasonography showed no lesions of the tendons or ligaments or joint effusion; there was no inflammation on the power doppler ultrasound. The MRI revealed no enthesopathy nor bone edema; on the other hand, it showed a thick synovial fringe extending the humeroradial fold, confirmed by the MRI-arthrogram. Treatment consisted in physiotherapy and a local injection of a corticosteroid suspension. Joint mobility was not improved but pain was sufficiently decreased to presently avoid arthroscopy. The presence of a humeroradial fold is frequently observed at autopsy or in the dissection room (from 80 to 100% of the reported series). It can be responsible for snapping, locking, pain and restricted mobility of the elbow. Elective pain is usually elicited by the pressure on the humeroradial joint space, beneath the lateral epicondyle. For diagnosis, MRI-arthrogram is the best radiological examination to perform, especially if the fold or the synovial fringe enters the joint space and if its thickness is above 3 mm. Symptoms can be improved by conservative treatment but may require an arthroscopic resection.

P 23

Comparison of two osteoporotic fracture management pathways: experience at 1 year

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Introduction: Osteoporosis presenting as low-impact fractures to traumatology units is often undiagnosed and under-treated. Results from the Osteocare study in Lausanne (a nurse based intervention, passive pathway) showed that only 19% of patients received management for osteoporosis, and in the literature [1], the rate is between 10–25%. We have evaluated a different management concept, based on the systematic assessment of patients with osteoporotic fractures during and after hospitalization (active pathway).
Methods: Inpatients admitted to the Department of Musculoskeletal Medicine for a fragility fracture were identified by a nurse according to a predefined questionnaire and were then clinically evaluated by a doctor. Based on the results, a management plan was proposed to the patients. Patients could choose between follow up either by their GP or by the Centre of Bone Disease of the CHUV. For patients who chose follow-up in our Centre, we assessed their adherence to medical follow-up 1 year inclusion. The results of patients who had been evaluated in our cohort between the 1 November 2008 and the 1 December 2009 were analysed.
Results: 573 inpatients received specific management of their osteoporotic fracture over 18 months. The mean age was 77 y (31–99), 81% were women (203 hip fractures, 40 pelvis fractures, 101 arm fractures, 57 vertebral fractures, 63 ankle fractures, and 25 others sites). During the study period, 303 patients received a proposition of a specific treatment. 39 (13%) chose a follow up with the GP, 19 (6%) dead and 245 (81%) preferred a follow up in our Centre. After 1 year, 166 (67%) patients are under follow up in our outpatient clinic.
Conclusion: With an active clinical pathway that starts during the hospitalization, consisting on a nursing evaluation followed by a medical consultation by an expert in osteoporosis, the adherence increased from 19% to 67% in terms of follow up. These results lead us to propose a consultation with a doctor experienced in osteoporosis after all osteoporotic fractures.
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P 24

Mid-diaphyseal cortical thickening in appendicular bone and scull with highly increased volumetric bone mineral density in a patient with diffuse pain syndrome

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A 36-year-old Pakistani woman was referred for evaluation of long-standing diffuse musculoskeletal pain. The veiled patient complained particularly about leg and lumbar back pain, occasional headache and generalized weakness. Clinical examination showed hyperlaxity and abdominal striae, but no dysmorphic features and functional deficits in the field of musculo-skeletal disorders. Laboratory examinations revealed a lack of 25-hydroxy-Vitamine D3, whereas 1,25-Dihydroxy-Vitamin, calcium, PTH, osteocalcin and crossLaps were normal, ESR slightly increased. Radiological imaging showed mid-diaphyseal cortical thickening of the femur and metacarpal bones. Scintigraphy was normal except for slightly degenerative changes. In the peripheral quantitative CT cortical bone area was increased to 80% of the total cross sectional area at femoral and metacarpal shaft, the volumetric BMD of cortices and trabeculae was increased. In the CT of the skull a thickening of the temporal and parietal cortices were found.
Discussion: Evidence of vitamin D deficiency and concealment as well as diffuse pain lead us initially to a hypothesis of osteomalacia, however this was refuted by normal calcium metabolism and high bone density. The findings of mid-diaphyseal cortical thickening in appendicular bone and scull together with a family history of reduced

strength in the legs and additional literature search pointed out to a rare syndrome, the Camurati-Engelmann Syndrome. Camurati-Engelmann Syndrome is a rare form of osteosclerosis caused by a genetic mutation on chromosome 19q13.1 leading to an over-expression of TGF-beta 1. Characteristic features are bone and joint pain especially in the legs with muscle weakness and sclerosis of the diaphyses of long bones and scull. Usually the symptoms begin on the legs and with progressive hyperostosis they can affect the base of the skull and the lower jaw. Treatment so far is only symptomatic and mostly consists of glucocortioids, in order to suppress TGF beta. Further investigations including genetics are scheduled. In conclusion, we report a for the first time data on volumetric bone mineral density in a patient with a possible Camurati-Engelmann Syndrome.

P 25

Cost-effectiveness of Tocilizumab in Switzerland: A Microsimulation Approach

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Introduction: Rheumatoid Arthritis (RA) imposes high costs on the affected patients as well as on the payers of the medical expenditures. Thus there are constant efforts to develop new drugs that are effective at reasonable costs. Tocilizumab is a humanised monoclonal antibody that binds to the interleukin-6 (IL-6) receptors, inhibiting IL-6-mediated proinflammatory activity. In Switzerland it is currently approved for patients who do not respond to traditional DMARDs or TNF-α-inhibitors. This study evaluates the cost-effectiveness of Tocilizumab as a treatment for RA in Switzerland.
Objectives: To adapt a model for cost-effectiveness evaluation developed in the English NHS to the Swiss context. To estimate the cost-effectiveness of Tocilizumab in Switzerland.
Methods: An individual simulation model, developed for the appraisal by the National Institute for Health and Clinical Excellence (NICE), is adapted to the Swiss context. The model simulates cost and utility progression over the life-time period of individual RA patients and allows to estimate direct and indirect costs per quality adjusted life year (QALY) gained. The simulation compares a standard sequence of treatments for RA without Tocilizumab with an alternative sequence where Tocilizumab is the initial agent. The model makes use of various data sources. Data on patient characteristics, drug efficacy and quality of life was extracted from clinical trials among patients with inadequate response to traditional DMARDs or to TNF-α-inhibitors. Treatment sequences were adapted to the Swiss standard of care for RA patients using information from the Swiss SCQM registry of RA patients as well as from clinical experts. Cost data was provided by health insurers.
Results: A standard sequence of treatments for RA in Switzerland and estimates of cost-effectiveness for Tocilizumab in the context of the Swiss healthcare system will be presented at the conference.

P 26

Immune response to influenza vaccination in children treated with methotrexate or/and tumor necrosis factor-alpha inhibitors

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Introduction: In children treated with methotrexate (MTX) and/or tumor necrosis factor-alpha (TNF-α) inhibitors, immunization is recommended due to greater risk of infections. It is still unclear if adequate antibody response to vaccinations can be achieved.
Methods: In a prospective open label study, we assessed seroconversion and seroprotection after influenza vaccination during 2 seasons (6 different strains) in 36 children treated either with MTX (n = 18), TNF-α inhibitors (n = 10) oder both (n = 8) and a control group of 16 immunocompetent children. In season 07/08, we included 31 children in the therapy group and 10 in the control group, in season 08/09 15 resp. 6 children in therapy resp. control group. Ten children of the therapy group were vaccinated as well in 07/08 as in 08/09. Influenza antibody titres were determined by haemagglutinin inhibition assay, before and 4-8 weeks after vaccination.
Results: Pre-vaccination seroprotection (titre ≥1:40 of ≥2 of 3 influenza strains) was present in 42% of the treatment group and 30% of the control group in season 07/08 and 33% resp. 50% in season 08/09. After vaccination, a protective titre was achieved in 87% of the treatment group and 90% of the control group in season 07/08 and 73% resp. 83% in season 08/09. Seroconversion was defined as the change from a negative titre (<1:40) to a protective titre (>1:40) with at least a 4-fold titer increase. This was documented in 57% resp. 50% (B strain), 46% resp 75% (A/H3N2 strain) and 58% resp. 80% (A/H1N1) in the treatment group resp. control group in season 07/08 and 50% resp. 67% (B strain), 44% resp. 60% (A/H3N2 strain) and 67% resp. 100% (A/H1N1 strain) in season 08/09. Safety evaluation of vaccination showed no serious adverse events.
Conclusion: Children under MTX and/or TNF-α-inhibitors can be safely and effectively immunized against influenza.

P 27

Effects of a multidisciplinary intervention program in back and neck pain patients absent from work – baseline data and effects on subjective workability, lifting capacity and sickness absence over 12 month

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Background: Sickness absence caused by back pain is a persistent and expensive health problem challenging most of industrial countries. Systematic reviews showed strong evidence, that multidisciplinary programs with a functional restoration approach including behavioural aspects and some relationship to the workplace improve function, but moderate evidence with respect to vocational outcomes. Furthermore, results depend on local (social) systems.
Objective: to evaluate the effects of a multidisciplinary intervention on subjective workability, lifting capacity and the number of sick days.
Methods: The study design is a randomised, observer blinded, controlled trial (RCT) comparing a multidisciplinary intervention strategy with usual care/ attention at two sites – Lausanne and Zurich, Switzerland. 6 large sized companies took part in the study. Subjects with more than 20 (complete absence) or 60 (partial absence) days of absence from work because of chronic back or neck-shoulder pain were clinically evaluated for exclusion reasons (age >58, specific backneck or shoulder disorder and any health condition not allowing a physical training). After informed consent, subjects got a clinical baseline assessment including questionnaires performance tests and were randomized stratified by companies (intervention group or controls). Assessment was repeated 4 month after inclusion, absence days were continuously observed until 12 month after inclusion.
Results: n = 80 (61% male), n intervention = 46, controls = 34, average age of 45 ± 8 y and absence duration of 68 ± 34 days. Groups didn't differ by age, gender and absence duration at inclusion (Pr 0.90 to 0.99). Subjective workability (WAI) at baseline was in average 26.1 ± 6.8 (intervention) respectively 23.8 ± 6.5 (controls, p >0.05), lifting capacity (lower PILE) 46.5 ± 9.5 kg (intervention) and 50.1 ± 13.1 kg (controls, p >0.5). 2nd assessment 24 ± 6.7 weeks after inclusion in both groups with complete data in 46 subjects (61% male, 23 interventions and 23 controls). WAI at 2nd evaluation showed a statistically not significant trend to positive change over time in the intervention group with higher values already at start, but no change in PILE could be recognized.
Conclusion: Due to the company based randomization procedure, more subjects were randomized to the intervention group by chance. Nevertheless, baseline data of groups were equal concerning age, gender and absence duration. WAI showed a positive trend over time in the intervention group. 12 month absence data are not completed yet due to the study process, but complete data will be available and presented at the congress.

P 28

Ultrasound Assessment in Rheumatoid Arthritis: Impact of US on Treatment

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Introduction: Ultrasound has proved to be more sensitive and more specific for detection of Synovitis in Rheumatoid Arthritis (RA) than clinical Assessment [1]. Although Ultrasound is being used more and more frequently in the assessment of RA, hardly anything is known about the direct impact on the treatment due to the US Examinations.
Methods: We added Questions about the direct impact of the US-assessment to the SONAR-SCQM Database. Questions to be answered by the treating physician after the US-Assessment were: 1) do the results of the joint Sonography influence your decision in therapy, yes/no. if yes question 2 was asked: do you treat a) more aggressively b) equal, c) less aggressively. 3) Does the result of the Sonography influence the willingness of your patient to accept changes in treatment?

Results: For 73 US Assessments (out of 104) answers about consequences of the US-Results were available. In 50 out of these 73 (68%) the results of Sonography had direct impact on the Treatment decision: 4 Patients (3.8%) were treated less aggressively, 26 (25%) more aggressively, in 20 patients (19.2%) the treatment was not changed. In 23 of the 73 Assessments (32%) the Sonography provided no additional information and had no Impact on treatment decision. In 60% (44 out of 73 Patients) the willingness of the patient to accept changes in the treatment was directly influenced by the US-assessment.
Conclusion: Obviously US-Assessment in RA has important immediate impact on patient management in different ways, most frequently leading into more aggressive, but sometimes as well into less aggressive treatment. The fact that in 60% results of US-Assessment influenced patient willingness for treatment changes is striking.
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P 29

Ultrasound Assessment in Rheumatoid Arthritis: Preliminary Results from the first 104 Patients included the SONAR-SCQM Database

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Introduction: The SCQM-Database and the widespread application of Sonography by Rheumatologists in Switzerland offer the unique opportunity to test and validate a Sonography US-Score within an ongoing quality management program. We report the preliminary results of the first 104 examinations in 94 Patients.
Methods: Between January 2009 and February 2010 all Swiss Rheumatologists performing ultrasonography were offered to attend up to the three educational courses for the assessment of Synovitis in RA. Definitions for Grading 0 (normal) up to 3 (severe synovial pathology) in B-mode and PWD-Mode with sample pictures for each grading and joint to be assessed were provided during the courses, with a poster handed out to all participants and on the SONAR Website [1]. The Scoring includes B-mode and Powerdoppler-Grading of MCP and PIP 2-5, wrist, elbow and knee bilaterally [2]. After the training all participants and teachers were motivated to assess their patients with RA by Sonography and to enter the sonographic and clinical assessments in the online SCQM-Database.
Results: Between August 2009 and April 2010 30 Rheumatologists performed 104 Examinations in 94 Patients, 10 Patients already had a follow up examination. (F = 82, M = 22, mean age 53 ± 12.6 years, mean disease duration 99.2 ± 96 months). 62.5% were positive for rheumatoid factor 48.1% positive for anti-CCP antibodies. 67.3% were on DMARDS, 38.5% on Biologics, 2 of which on 2 Biologics. Mean SJC was 4.6 ± 5.7 and TJC 5.3 ± 5.6; mean DAS (CRP and ESR) was 3.6 ± 1.5. Mean B-mode Score was 12.9 ± 10.4; mean PWD-Score 3.9 ± 4.3. High positive correlations were found for B-mode Scoring and SJC (0.722) as well PWD-score (0.692), moderate correlation for B-mode Score and DAS (DASESR: 0.505), (DASCRP: 0.537) as well as PWD-score with SJC (0.518) and DAS (DASESR: 0.460). Also TJC showed significant but lower correlation with B-Mode Score (0.392) as well as PWD-Score (0.281).
Conclusion: Sonographic Assessment of RA Diseaseactivity with the proposed US-Scoring System within the ongoing SCQM-Database is feasible and valid. As in previous studies TJC shows lowest correlation with US compared to SJC and the composite measure DAS [3]. Inclusion of more patients and prospective follow up will clarify if US-assessment has prognostic value and adds any meaningful information for clinical decision making.
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Free communications

HP 1

Perceived functional ability assessed with the Spinal Function Sort: Is it valid for European Rehabilitation Settings in patients with non-specific low back pain?

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Background: The use of self-reported measures is limited by literacy level and depends on linguistic abilities. Text-based questionnaires are therefore often impossible to administer in European rehabilitation settings treating patients with different mother tongues. A possible approach to overcome this problem is the use of picture-based questionnaires such as the Spinal Function Sort (SFS) assessing perceived ability to perform work tasks that involve the spine. Its psychometric properties were investigated in patient populations from the USA and Australia. No studies have been performed investigating the validity of the SFS in a European rehabilitation setting.
Objectives: To test the validity of the SFS in a European rehabilitation setting treating patients with non-specific low back pain (NSLBP).
Methods: This validation study is embedded within a RCT investigating two in-patient exercise programs aiming for early return to work (RTW). Eligible were patients with NSLBP, 20–55 years old, and at least 6 weeks of sick leave. Measurements of body functions, work-related activities and personal beliefs were taken by a blinded research assistant. RTW at 3 and 12 month follow-up was assessed through to the family physician and employer. Internal consistency was assessed by item-total correlations and Cronbach's alpha. Principal component analysis was used to assess the unidimensionality of the instrument. Concurrent validity was assessed by comparing the SFS scores with body function, work-related activity and personal beliefs with Spearman's correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of the SFS scores at discharge for RTW at 3 and 12 month follow-up. Responsiveness was assessed in the two treatment groups with the standardised response mean (SRM).
Results: 170 patients from 10 different European countries were included in this study finding a high internal consistency shown by a Cronbach's alpha of 0.98, reasonable evidence for unidimensionality, spearman correlations of >0.6 (p = 0.001) with work activities, and discriminating power for work status at 3- and 12 month by ROC curve analysis (area under curve = 0.760 (95%CI: 0.689–0.822) resp. 0.787 (95%CI: 0.712–0.851). The SRM within the two treatment groups was 0.18 and –0.31.
Conclusion: Perceived functional ability can validly be assessed with the SFS in a European rehabilitation setting treating patients with NSLBP and is predictive for RTW.

HP 3

Is the Work Ability Index useful to measure the absence days in ankylosing spondylitis patients?

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Aims: The incapacity for work in people with ankylosing spondylitis (AS) reflects a socioeconomic problem and lies in the range of 3–50% in European countries [1]. The Work Ability Index (WAI) is applied to measure the subjective ability to work.
Aims: to investigate the incapacity for work in terms of absence days in a study-sample with AS in Switzerland; to evaluate whether the WAI reflects the absence from work; and whether the subjective incapacity for work decreases after the intervention.
Methods: A randomised controlled trial evaluating the effect of cardiovascular training in people with AS. The WAI and questions about work absence days, part-time work, and disability pension were administered at baseline and after the three-month intervention. Spearman-correlation was performed between the WAI and absence days in a subgroup of AS patients, who had at least one or more absence days.
Results: Of a total of 106 people (mean age 48.7 (SD ± 12.3)), 14 were retired due to age. Of the other 92 people, 14 received a full or partial disability pension and 78 were in the working process. The mean of the absence days per year of the 78 people due to all reasons and due to AS was 23.6 days (SD ± 50.3) and 17.9 days (SD ± 43.7), respectively. If the disability in the 14 people receiving a disability pension was expressed in days of absences and added to the absences of all working participants (n = 92), then the mean was 47.9 days (SD ± 79.1) due to all reasons. ANOVA could not reveal that WAI scores changed after 3 months. Spearman-correlation between the WAI and absence days was r = –0.701 (p <0.01) (n = 58).
Conclusion: Incapacity for work of our participants was equal to pan-European studies [1, 2], but larger than in another Swiss cohort [3]. The WAI-score does represent the absence days in the subgroup of patients with absence days. Hence, the WAI could be used in economic studies to estimate the absence days and to evaluate the indirect costs in patients with AS who have sick leave.
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