Results: Sera from 43 consecutive limited cutaneous (lc) SSc subjects, 44 early (<3 years from disease onset) diffuse cutaneous (dc) SSc patients and 20 age, gender and ethnicity matched healthy controls were analysed. There were no differences between lcSSc and dcSSc patients in terms of gender or ethnicity, age at disease onset or sample collection. As expected the lcSSc subjects more often had overlap syndromes compared to the dcSSc ones (30% v 11%, p<0.001), and had higher frequency of anti-centromere antibodies (49% v 2%, p<0.001), while anti-RNA polymerase III antibodies were found only in the dcSSc cohort (32% v 0%, p < 0.001). The mean ± SD disease duration at sample collection was significantly longer for the lcSSc cohort (132 ± 83 months) compared to 22 ± 12 for dcSSc cohort. There were no differences between the two subsets in frequency of clinically significant internal organ disease. MMP7 levels varied between 1.1 and 84.5 ng/mL (mean ± SD 8.8 ± 8.5, median 6.7 ng/mL) while MMP9 levels were measured between 54 and 5405 ng/mL (mean ± SD 651.9 ± 562, median 548.6 ng/mL). There was no correlation between MMP7 and MMP9 levels.

We found no gender or ethnicity differences in the levels of MMP7 and MMP9. Compared to healthy controls SSc patients had altered levels of both MMP7 and MMP9 - mean MMP7 level was 10.2 ng/mL for dcSSc, 8.9 ng/mL for lcSSc and 4.6 ng/mL for control groups (p<0.001) while mean MMP9 level was 892 ng/mL for dcSSc, 460.8 ng/mL for lcSSc and 607.2 ng/mL for controls (p < 0.001). The only significant association with autoantibodies we observed was for anti-topoisomerase I antibody (ATA) positive patients who had higher MMP7 levels (mean 14.3 ng/mL) compared to ATA negative subjects (8.23 ng/mL), p = 0.049. MMP7 levels were also higher in subjects with clinically significant (cs) PF (13.8 ng/mL) compared to those without (8.13 ng/mL, p = 0.017) and in subjects who developed renal crisis (16.5 ng/mL) compared to those who did not (8.8 ng/mL, p = 0.016). There was no association of MMP7 and MMP9 levels with pulmonary hypertension, cardiac scleroderma or severe digital vasculopathy. We also found no correlation between mRss and MMP7 or MMP9 levels.
Conclusions: Both MMP7 and MMP9 levels were higher in dcSSc subjects compared to lcSSc subjects or controls. Higher MMP7 levels were also associated with ATA positivity, development of csPF and SRC. Both MMP7 and MMP9 may have potential as biomarkers in SSc and further study is warranted.
Disclosure statement: The authors have declared no conflicts of interest.

243.   ELEVATED IL-6 LEVELS ASSOCIATE WITH POOR CLINICAL OUTCOME AND MAY PROMOTE FIBROSIS IN EARLY dcSSC

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Background: We previously showed that thrombocytosis may identify a subgroup of diffuse SSc with increased IL-6 and high modified Rodnan skin score (mRSS). We assessed the predictive value of high IL-6 in these patients and its role in driving fibrosis in SSc.
Methods: IL-6 levels were assessed with immunohistochemistry and Western blot analysis. Skin biopsies from patients with early dcSSc and thrombocytosis(n = 10,mean platelet:472x109/L,disease duration, Mean ± SEM:35 ± 9.5 months),established dcSSc(n = 8,mean platelet:293x109/L, disease duration:128 ± 22) and controls(n = 12) were used. IL-6 levels were measured in the supernatant from cultured SSc fibroblasts and the effect of anti-IL6 receptor antibody on collagen production was examined in normal fibroblasts stimulated with IL-6.

To investigate the link between IL-6 levels and clinical outcome serum IL-6(in pg/ml) from 39 patients with dcSSc (74% female) was quantified by ELISA. The dcSSc cases were categorised into high IL-6(≥10 pg/ml) and low IL-6 cohorts. Association between IL-6 levels and mRSS at 36months from disease onset was determined by Pearson's correlation. Mean difference of mRSS between the two cohorts of IL-6 levels over the 36-month period was compared by Student t-test. Difference in survival between cohorts was examined using Kaplan-Meier methods.
Results: There was greater dermal IL-6 expression in patients with early dcSSc than other subgroups. Strong immunostaining for IL-6 was associated with dermal fibroblasts, vascular structures and mononuclear inflammatory infiltrate in 80% of patients with early dcSSc. Moderate vascular expression for IL-6 was observed in 33% of healthy controls. Similar expression pattern was observed in 25% patients with established dcSSc with weak staining for IL-6 in dermal fibroblasts and inflammatory infiltrates.

IL-6 was elevated in the supernatant from cultured SSc fibroblasts (n = 3) by 17-fold (Densitometric Image Unit, DIU p < 0.05). In addition, collagen production was upregulated by 7-fold in SSc fibroblasts and

similar induction by recombinant IL-6(20 ng/ml) was observed in normal fibroblasts (17.94 + 3.41 vs 2.18 + 1.85 DIU control, p < 0.05). This was partially abrogated with neutralising antibody against IL-6 receptor (4.26 + 2.07 DIU, p < 0.05).

Serum IL-6 level at presentation positively correlated with mRSS at 36 months follow-up in a subgroup of dcSSc cases (r = 0.81, p < 0.01, n = 16). There was a significant difference in mean mRSS between the two groups with differential IL-6 expression (10.9, 95% Confidence interval, 3.8, 18.2, p < 0.01). Kaplan-Meier analysis showed that the 5-year survival was 93% and 81% in the group with low and high IL-6 levels respectively (p = 0.02, log rank test).
Conclusions: This data confirms upregulation of IL-6 in some cases of early dcSSc and support the potential role of IL-6 as a surrogate marker for clinical outcome in SSc. Our study also suggests that IL-6 may a logical target for therapy in this subset of patients.
Disclosure statement: The authors have declared no conflicts of interest.

Spondylarthropathies (including psoriatic arthritis)

244.   VALIDITY OF COLOUR DOPPLER AND SPECTRAL DOPPLER ULTRASOUND OF SACROILICAC JOINTS AGAINTS PHYSICAL EXAMINATION AS GOLD STANDARD

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Background: Sacroiliac joints (SJ) involvement is a distinctive and charasteristic feature of Spondyloarthritis (SpA) and x-ray is the test routinely used to make a diagnosis. However, x-ray reveals late structural damage but cannot detect active inflammation. The objective of this study was to assess the validity of Doppler ultrasound in SJ.
Methods: Prospective blinded and controlled study of SJ, in which three populations were compared. We studied 106 consecutive cases, who were divided into three groups: a) 53 patients diagnosed with SpA who had inflammatory lumbar and gluteal pain assessed by a rheumatologist; b) 26 patients diagnosed with SpA who didn't have SJ tenderness and had normal physical examination; c) control group of 27 subjects (healthy subjetcs or with mechanical lumbar pain). All patients included that were diagnosed with SpA met almost the European Spondyloarthropathy Study Group (ESSG) classification criteria. Physical examination of the SJ included: sacral sulcus tenderness, iliac gapping, iliac compression, midline sacral thrust test, Gaenslen's test, and Patrick s test were used as gold standard. Both SJ were examined with Doppler ultrasound (General Electric Logiq 9, Wauwatosa WI, USA) fitted with a 9-14 Mhz lineal probe. The ultrasonographer was blinded to clinical data.

Doppler in SJ was assessed as positive when both Doppler colour and resistance index (RI) < 0.75 within the SJ area were present. Statistical analysis was performed estimating sensitivity and specificity against gold standard. The Kappa correlation coefficient was used for reliability study.
Results: 106 cases (53 female, 55 male; mean age 36 10 years) were studied. There were no statistical differences between groups related to age or sex. Physical examination of SJ was positive in 38 patients (59 sacroiliac joints). US detected Doppler signal within SJ in 37 patients (58 SJ): 33 of them were symptomatic SpA (52 SJ), one of them were asymptomatic SpA (1 SJ) and one was a healthy control (1 SJ). The accuracy of US when compared to clinical data as gold standard at subject level in the overall group was: sensitivity of 68.6% and specificity of 85.7%, positive predictive value of 70.5% and negative predictive value of 84.5%. A positive likelihood ratio of 4.8, a negative likelihood ratio of 0.36 and a kappa coefficient of 0.55 were achieved.
Conclusions: Doppler US of SJ seems to be a valid method to detect active SJ inflammation.
Disclosure statement: The authors have declared no conflicts of interest.

245. EUROQOL-REPORTED HEALTH DISABILITY DEMONSTRATES REDUCED QUALITY OF LIFE REMAINING CONSTANT OVER TIME IN ESTABLISHED PSORIATIC ARTHRITIS

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Background: Psoriasis (PsO) and Psoriatic arthritis (PsA) are known to have a significantly detrimental effect on health related quality of life (HRQoL). The EuroQol (EQ5D) has been used in a number of PsA clinical trials, distinguishes well across levels of PsA severity, and demonstrates utility gain in patients started on anti-TNF therapy within the first few weeks, sustained over time. Our objective was to measure health related quality of life in PsA using the EQ5D and assess change over time; dependent on age, gender, disease duration and anti-TNF treatment.

Methods: The EQ5D is a self reported questionnaire describing health-related quality of life consisting of five descriptive questions (EQ5D) converted into a single summary index using UK valuation index and a visual analogue scale (EQ5Dvas) from 100 as best imaginable health and 0 worst imaginable health. 520 patients were sent EQ5D questionnaires at six month intervals between 1/2008 and 1/2010. 317 patients returned questionnaires. 287 patients completed the EQ5D fully on at least one time point. 184 patients completed EQ5D at two or more time points. HAQ was available for 173 patients and DLQI for 24 patients. The first and last questionnaires were compared, mean interval 1.2yrs (443 days, range 4-882). Comparisons over time were made with paired t test or Wilcoxon rank as appropriate. Correlations were performed using the Pearson correlation coefficient.

Results: Of the 287 patients the mean age was 66yrs (median 70, range 20-86), 50.2% male (n = 144) 49.8% female (n = 143) and disease duration mean 16.9yrs (range 0-57yrs). The mean EQ5Dvas was 68.1 (Standard Deviation 23, Standard Error of Mean 1.3), male 68.8 (SD 23.4 SEM 1.9), female 67.5 (SD 28.8, SEM 1.9). Results of the 184 patients who completed questionnaires at two time points are reported in Table 1. HAQ (Minimally Important Difference [MID] 0.22) and DLQI (MID between 2.2 and 3.1) demonstrated statistical but not clinically significant improvement. There was no change in EQ5D or EQ5Dvas over time between age, gender, disease-duration or anti-TNF treatment. EQ5Dindex demonstrated good correlation with the HAQ (-0.56) and DLQI (r = −0.59) significant at p < 0.01.

Conclusions: Health related quality of life as measured with the EQ5D and HAQ demonstrates reduced quality of life in PsA patients and this impairment remains constant over time irrespective of age, gender, disease-duration or therapy. However, our study will not have captured early phase improvement following treatment initiation that we are now studying prospectively.

Disclosure statement: The authors have declared no conflicts of interest.

TABLE 1. EQ5D, HAQ and DLQI 1.2 year interval (range 4-882 days)

Outcome	Mean baseline	Mean follow up	Mean change	SD	SEM	t	Sig (2tailed)
EQ5Dvas (n = 184)	66.3	64.7	1.58	23.79	1.75	0.90	0.36
EQ5Dindex (n = 184)	0.60	0.63	−0.03	0.27	0.20	−1.49	0.13
HAQ (n = 173)	1.02	0.92	0.10	0.56	0.04	2.52	0.01
DLQI (n = 24)	4.20	2.41	1.79	3.84	0.78	2.2	0.03

Paired t-test

246. EMPLOYMENT STATUS IN A GROUP OF PATIENTS WITH ANKYLOSING SPONDYLITIS TAKING PART IN A CLINICAL TRIAL BETWEEN 2004-2006

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Background: Patients with many rheumatological conditions develop a degree of work disability or even leave employment. In rheumatoid arthritis a 2.0 to 2.7 fold increased risk of being unable to work has been reported. In other rheumatological conditions work disability rates of between 20 and 40% have been reported. In 2008 a UK wide survey of 612 patients with ankylosing spondylitis (AS) reported that only 60.7% of working age patients were in employment, approximately 14% lower than the UK national average at that time. A similar employment rate was reported in a Dutch study and other groups have reported figures of between 10 and 40%. The analysis of employment data has become of more interest recently and is increasingly considered when treatment and funding decisions are made. We present the baseline employment statistics of a group of AS patients recruited to the BIAS (Bisphosphonates in AS) trial between 2004-2006. This data provides UK employment data just prior to anti-TNF therapy becoming available nationally in the NHS. The BIAS study results are awaiting publication.

Methods: 180 patients recruited from 6 UK rheumatology departments met refined modified New York criteria. There was no upper age limit but all were >21 years.

Results: 165/180 patients recruited were of working age. 125/165 (76%) were in employment, but only 57.5% were working full time. 33/165 (20%) were receiving incapacity benefits. 57/165 (40.7%) of those working had a BASDAI >4 and 37 of those were working full time. These figures should be compared to the 2004-6 average UK unemployment rate which was 4.7%.

In those who were in work there was no significant correlation between hours worked and BASDAI, BASFI, or BASMI scores.

Conclusions: The ability to work for patients with AS is affected at both an individual and societal level, and should be considered as integral to decision making at both levels. Epidemiological data, as reported here, is required to inform such decisions.

These results support previous reports that patients with AS are less likely to be able to work than the general population. However it is interesting that unemployment levels in this cohort are lower than those described only 2 years later in a large UK based epidemiological survey. This may have been influenced because patients with disability preventing them from working may also have felt unable to commit to taking part in a trial. In addition there were low levels of unemployment in the UK during data collection. In times of increasing unemployment those with less severe disability might consider taking early retirement or redundancy if offered. It also gives a snapshot of employment at a time before anti-TNF alpha therapy was widely available. As employment data is increasingly considered when treatment and funding decisions are made it is a helpful addition to the literature available when considering the impact that new therapies have had.

Disclosure statement: The authors have declared no conflicts of interest.

247. THE EFFICACY OF ANTI-TNF DRUGS IN A REAL-LIFE POPULATION WITH ANKYLOSING SPONDYLITIS IS SUSTAINED FOR UP TO SIX YEARS

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Background: The efficacy of anti-TNF drugs in ankylosing spondylitis (AS) has been well-established by clinical trials. However, less is known about their long-term effectiveness in routine clinical care.

Methods: All patients prescribed anti-TNF drugs for AS before October 2006 were included. Data were obtained from our department's biologics register, supplemented by case note review. Outcome measures included Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and CRP.

Results: A total of 61 patients were identified, of whom 52 were currently taking anti-TNF drugs. Three patients (5%) discontinued because of side effects and 8% because of inefficacy. Seventeen patients (28%) switched to another anti-TNF drug because of inefficacy or side effects, with 14 of these (82%) continuing the second drug in the long-term. Baseline data were available for 46 current patients (83% male, median age 53 years (IQR 42-58), median disease duration 19 years (IQR 12.75 - 24.5). The outcome measures at each time point are recorded in Table 1. Mean baseline BASDAI was 6.88 (95% CI 6.47, 7.29), falling to 3.53 (2.86, 4.2) at 1 year and 3.14 (2.52, 3.76) at 4 years. For a subset of patients, data was available for 5 years (mean BASDAI 2.23 (1.48, 2.98); n = 20) and 6 years (mean BASDAI 2.20 (1.61, 2.79); n = 13) of treatment. A similar trend was seen in BASFI, with mean baseline 6.67 (6.16, 7.18), reducing to 4.10 (3.34, 4.86) at 1 year, 3.84 (3.11, 4.57) at 4 years and 3.04 (2, 4.08) at 6 years (n = 11). Mean CRP also fell from a baseline value of 24.8 (18.04, 31.56) mg/L to 7.3 (4.96, 9.64) mg/L at 1 year, 7.73 (4.69, 10.77) mg/L at 4 years and 4.77 (3.25, 6.29) mg/L at 6 years (n = 13).

TABLE 1.

Mean (95%CI)	Baseline n = 46	1 year	2 years	3 years	4 years n = 46	5 years n = 20	6 years n = 13
BASDAI	6.8 (6.47, 7.29)	3.53 (2.86, 4.2)	3.42 (2.73, 4.11)	3.0 (2.34, 3.66)	3.14 (2.52, 3.76)	2.23 (1.48, 2.98)	2.2 (1.61, 2.79)
BASFI	6.67 (6.16, 7.18)	4.10 (3.34, 4.86)	4.14 (3.36, 4.92)	3.82 (3.06, 4.58)	3.84 (3.11, 4.57)	3.30 (2.20, 4.41)	3.04 (2.0, 4.08)
CRP (mg/L)	24.8 (18.04, 31.56)	7.3 (4.96, 9.64)	8.5 (4.78, 12.22)	6.82 (3.92, 9.72)	7.73 (4.69, 10.77)	4.35 (2.77, 5.93)	4.77 (3.25, 6.29)

Conclusions: Although the greatest improvements in BASDAI, BASFI and CRP are seen after 1 year of anti-TNF treatment, this response is sustained for up to 6 years in a real-life population with AS.

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248. SOCIODEMOGRAPHIC DIFFERENCES BETWEEN PATIENTS WITH PSORIATIC ARTHRITIS: A RHEUMATOLOGY OUTPATIENT BASED COMPARISON OF INDIAN GUJARATI AND CAUCASIAN PATIENTS

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Background: There is a paucity of information regarding whether ethnicity influences the presentation of psoriatic arthritis (PsA). Leicester has a large Indian Gujarati population, but little is known about the epidemiology of PsA in this group. The purpose of this study was to examine whether sociodemographic factors in this group of patients differ from those in Caucasian patients.

Methods: 60 Gujarati Indians and 60 Caucasians who were diagnosed with PsA according to the ACR criteria were recruited consecutively from the rheumatology outpatient clinic. They were assessed using a standardized questionnaire comprising of previously validated tools and a clinical examination was carried out. The following data were collected: age, gender, alcohol intake, smoking status, pain by visual analogue scale, disability measured using the Stanford Health assessment Questionnaire, and occupation and employment. Participants were also asked about the number of family members at home, the number of people who help them at home, and the number of state benefits they were in receipt of.

Results: The mean age of the 2 groups of patients did not differ (50.7 years for the Gujarati Indians and 50.7 years for the Caucasians). The Gujarati Indian group comprised of 36 (60%) males and 24 (40%) females. The Caucasian group comprised of 33 (55%) males and 27 (45%) females. Alcohol consumption was significantly higher in Caucasians (n = 48, 80.0%) compared to the Gujarati Indians (n = 28, 46.7%, p < 0.0001). Also significantly more Caucasians (n = 37, 61.7%) were current or previous smokers compared to the Gujarati Indians (n = 17, 28.3%, p = 0.0004). The Gujarati Indians had significantly more disability, Pain, rate of unemployment and higher claims for benefits (Table 1).

Conclusions: Gujarati Indian patients with PsA have more disability and pain, compared to Caucasian patients, despite having more people at home who help them, and despite having a healthier lifestyle in terms of alcohol intake and smoking history. This group also has higher levels of unemployment. There is a suggestion that the Gujarati Indian patients may be more socially deprived as indicated by fewer years of formal education and the higher number of social benefits claimed by this group. These findings need to be confirmed by community-based studies.

Disclosure statement: The authors have declared no conflicts of interest.

TABLE 1.

Variable	Gujarati Indians	Caucasians	p value (significant if p < 0.05)
Pain by VAS	51.6	34.9	<0.0001
HAQ score	0.9	0.8	0.039
Number of family members at home	3.0	1.7	0.0001
Number of family members who help	1.0	0.4	0.001
Years of formal education	11.8	17.0	0.749
Number Unemployed	21	10	0.036
Number of state benefits received	1.0	0.6	0.079

249. MODIFICATION OF MINIMAL DISEASE ACTIVITY SCORE BY REPLACEMENT OF PASI WITH PGA FOR ADALIMUMAB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS

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Background: A new outcome scoring method for measuring a state of minimal disease activity (MDA) in various clinical manifestations of psoriatic arthritis (PsA) has recently been proposed. The Psoriasis Activity and Severity Index (PASI) or body surface area (BSA) are among the criteria used in this new MDA method. Independent from the MDA score, the Physician's Global Assessment of psoriasis (PGA) was reported to be a more appropriate measure than the PASI for patients with mild psoriasis (Ps).

Methods: We compared the performance of the MDA with PASI or PGA using patient data from a 24-week, randomized, placebo-controlled trial (ADEPT) of adalimumab (ADA) for the treatment of active PsA. MDA is defined by achieving 5 of the 7 following criteria: tender joint count (0-78) ≤1, swollen joint count (0-76) ≤1, PASI ≤1 or BSA ≤3%, patient pain on a 0-100-mm visual analog scale (VAS) ≤15, Patient's Global Assessment of disease activity (0-100-mm VAS) ≤20, Health Assessment Questionnaire score ≤0.5, and tender entheseal points ≤1.1 Only patients from ADEPT with PsA and active Ps (≥3% affected BSA) were included in this post hoc analysis. A heel-limited enthesitis score (0-4) and PASI ≤1 were used for calculation of MDA at week 24. We then replaced the PASI ≤1 criterion with PGA ''Clear'' (MDA_mod1) and with PGA ''Clear or Almost Clear'' (MDA_mod2). The performance of PASI and PGA in the MDA were compared using combined data from ADA- and placebo-treated patients using the kappa coefficient.

Results: Baseline characteristics for MDA score criteria were similar between the ADA and placebo treatment groups. At week 24, MDA/ MDA_mod1/MDA_mod2 was achieved by 40%/38%/40% of 60 ADA-treated patients and 7%/5%/8% of 60 placebo-treated patients (P < 0.001 for all treatment comparisons). Use of PASI ≤1 yielded results similar to those obtained using PGA ''Clear'' or PGA ''Clear or Almost Clear'' at week 24. Kappa coefficients showed that PGA ''Clear or Almost Clear'' agreed slightly better with PASI ≤1 than did PGA ''Clear'' (Table 1).

Conclusions: A new scoring method to assess Minimal Disease Activity (MDA) in PsA demonstrated that significantly more adalimumab-treated than placebo-treated patients achieved an MDA state by week 24 in the ADEPT trial (40% vs. 7%, P < 0.001). Performance of the new MDA scoring method was not altered when PASI ≤1 was replaced with PGA ''Clear'' or with PGA ''Clear or Almost Clear.'' More than one-third of patients with PsA who had both active arthritis and active Ps achieved MDA after 24 weeks of ADA treatment.

Disclosure statement: S.K. is a contract employee of Abbott. H.K. and M.O. are employees of Abbott and may own Abbott stock or stock options. P.M. has received research grants and consultancy fees from, and is/has been a member of speakers' bureaus for Abbott, Amgen, Biogen Idec, Bristol-Myers Squibb, Centocor, Genentech, UCB and Pfizer, and has received a research grant and consultancy fees from Roche.

TABLE 1.

PASI ≤1	PGA ''Clear''		Observed Agreement, %	Kappa	PGA ''Clear or Almost Clear''		Observed Agreement, %	Kappa
	Yes	No			Yes	No		
Yes	20	15	87	0.65	34	1	86	0.69
No	0	83			16	67		

250. REGIONAL AUDIT OF THE USE OF ANTI-TNF AGENTS FOR THE TREATMENT OF ANKYLOSING SPONDYLITIS IN RELATION TO NICE GUIDELINES

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Background: Adalimumab and etanercept are recommended by NICE (TA 143) as treatment options for adults with severe active ankylosing spondylitis (AS) provided they fulfill clearly defined clinical criteria. These treatments should be monitored for continued efficacy by reassessment at regular predefined intervals. Treatment should only be continued in the presence of an adequate response as defined in the NICE guidance. The aim of this regional audit was to assess compliance with these guidelines in secondary care rheumatology departments.

Methods: Following a pilot audit at two participating centres, a proforma questionnaire, BASDAI and spinal VAS was sent to 17 rheumatology centres across the East and West Midlands. Data was collected prospectively over 4 weeks from patients with AS attending general or specialised out-patient clinics and retrospectively in patients treated with anti-TNF but not attending follow up during the 4 week observation period.

Results: 331/416 (80%) of patients meeting the modified New York criteria for AS were male.

97/238 (41%) of patients recruited prospectively were currently receiving anti-TNF therapy: 44(45%) adalimumab, 49(51%) etanercept and 4 (4%) infliximab. 11/238 (5%) of patients had previously received anti- TNF therapy. 130/238 (55%) of patients had not received anti-TNF. 58/130 (45%) of these fulfilled NICE BASDAI/painVAS criteria, of these: 14/58 declined treatment, 11/58 had contraindications, 22/58 were being assessed to start anti-TNF, 10/58 were not treated on clinician's judgement and 1/58 had funding problems. Reviewing all patients on anti-TNF, pre-treatment assessments 12 weeks apart were documented in 154 (55%) patients on anti-TNF with a further 73 (26%) having these at a 4 week interval. Prior treatment with two or more NSAIDS had been documented in 249 (89%) patients. Initial assessments 12 weeks after anti-TNF introduction were conducted in 162 (58%) patients: 48 (17%) patients had a documented inadequate response at this initial assessment and of these only 9 (19%) had their treatment discontinued. Regular twelve weekly disease activity assessments were occurring in 128 (46%) patients.

Conclusions: This audit demonstrates areas of sub-optimal compliance with anti-TNF therapy NICE guidance in AS. In the pre-treatment assessment for anti-TNF therapy, a significant proportion of patients were being assessed in accordance with BSR guidance as opposed to NICE guidance. The proportion of patients being assessed at 12 weeks after treatment initiation was sub-optimal. Less than 20% of patients with a defined inadequate response at 12 weeks had their treatment discontinued. Less than half of the patients received regular 12 weekly assessments. Reasons for this lack of compliance require further evaluation.

Disclosure statement: The authors have declared no conflicts of interest.

251. INVESTIGATING THE USE OF THE NEW RA CLASSIFICATION CRITERIA IN PSORIATIC ARTHRITIS

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Background: The new ACR-EULAR classification criteria for rheumatoid arthritis (RA) have been developed in undifferentiated arthritis populations. They state that the criteria should only be applied in patients with synovitis not better explained by another disease, but do not state how alternative diagnoses should be excluded. The aim of this study was to investigate whether the new ACR/EULAR criteria for early RA are robust in excluding PsA.

Methods: The new ACR/EULAR criteria for early RA and the Moll&Wright and CASPAR criteria for PsA were applied to cases of early PsA (less than 24 months symptom duration), early RA and other forms of early inflammatory arthritis who were all disease-modifying anti-rheumatic drug naive. Gold standard diagnosis was confirmed by a consultant rheumatologist. All joints required for the ACR/EULAR criteria were assessed.

Results: 111 early PsA cases, 82 early RA cases and 29 other early arthritis controls (undifferentiated arthritis n = 13, spondyloarthritis n = 9, inflamm OA n = 4, crystal arthritis n = 3) were recruited. The sensitivity of the ACR/EULAR criteria (score ≥ 6) in classifying early RA was 91%. The specificity for the criteria when considering all other diagnoses was 53%. When considering the specificity only for PsA, it was lower at 48%. When comparing classification criteria for RA and PsA, none of the RA patients met the PsA criteria (either Moll&Wright or CASPAR), and only 1 of the other inflammatory arthritis patients fulfilled these criteria. The majority of PsA patients who met the RA classification criteria also met the PsA classification criteria (48 of 58). The 10 patients who met the ACR/EULAR criteria but not the CASPAR criteria all scored 2 CASPAR points.

Conclusions: The new ACR/EULAR criteria are sensitive at identifying early RA but are not specific when considering psoriatic arthritis. The majority of PsA patients met the criteria due to high joint counts despite negative RF and psoriasis. The ACR/EULAR criteria must be used with caution in an early arthritis population particularly when patients have evidence of skin or nail psoriasis.

Disclosure statement: The authors have declared no conflicts of interest.

TABLE 1.

ACR/EULAR criteria components fulfilled (% with feature)	Early PsA (n = 111)	Early RA (n = 82)	Other controls (n = 29)
synovitis of at least 1 joint	92	96	83
1 large joint	46	50	45
2-10 large joints	53	46	28
1-3 small joints	23	11	28
4-10 small joints	41	37	35
>10 joints including 1 small joint	30	60	7
Neg RF and ACPA	94	20	79
low positive RF or ACPA	4	10	14
high positive RF or ACPA	3	71	7
duration over 6 weeks	99	98	83
raised CRP or ESR	48	77	63

252. EPITOPE MAPPING OF A NOVEL B27-SPECIFIC ANTIBODY

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Background: The major histocompatibility complex (MHC) allele, HLA-B27 (B27), is strongly associated with the development of spondyloarthritis. The classic immunological function of MHC molecules is to present peptides, in a heterotrimeric complex with beta-2-microglobulin (β2m), to CD8+ T cells. However, B27 has been shown to form non-classical β2m-free homodimers at the cell surface. It has been suggested that there may be a pathogenic role for cell surface B27 homodimer interactions with natural killer (NK) cell receptors, such as leukocyte immunoglobulin-like receptors (LILRs) and killer immunoglobulin-like receptors (KIRs). Here, we have prepared the groundwork for future investigation of the role of B27 on the cell surface by measuring the affinity and specificity of a heavy chain specific antibody (HC-10) and a candidate B27 homodimer-specific monoclonal antibody (HD6) to the B27 homodimer.

Methods: 1) B27 was expressed in E.Coli, purified and then refolded by limiting dilution in presence of peptide. 2) Isolation of refolded homodimer protein complexes was conducted by gel exclusion chromatography 3) Surface Plasmon Resonance (SPR) was used to analyse the binding specificity and affinity of HD6 for B27 homodimer 4) Epitope mapping using Trypsin Digest of B27 and then Mass spectroscopy was used to identify a possible binding region of HD6 to the B27 homodimer.

Results: Using SPR, HD6 is shown to bind to the B27 homodimer, but not to B27 heterotrimers, HLA-A3 heterotrimers or HLA-G homodimers. Furthermore, HD6 is shown to bind with a high affinity to B27

homodimers, demonstrating a KD of 280 nM. In addition, SPR competition experiments and Mass Spectroscopy based epitope-mapping experiments have allowed the development of a model for HD6 binding to the B27 homodimer.

Conclusions: These findings are important as they improve our understanding of the specificity and affinity of the HD6 antibody. This is vital in our assessment of HD6 and its use in in vivo experiments, and as a potential therapeutic agent.

Disclosure statement: The authors have declared no conflicts of interest.

253. DISCONNECT BETWEEN DISEASE ACTIVITY AND JOINT SPACE NARROWING FOR PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH ADALIMUMAB PLUS METHOTREXATE BUT NOT FOR PATIENTS TREATED WITH METHOTREXATE ALONE

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Background: Joint space narrowing (JSN) is a critical outcome in rheumatoid arthritis (RA) because it is more strongly associated with disability than bone erosions. The relationships between disease activity, treatment, and JSN have not been fully explored in psoriatic arthritis (PsA).

Methods: This post hoc analysis explored whether treatment with adalimumab (ADA), with or without methotrexate (MTX), resulted in greater inhibition of JSN than placebo (with or without MTX) in PsA patients. ADEPT was a 24-week, randomized, placebo-controlled trial of ADA for the treatment of active PsA. Treatment groups were randomized following stratification of subjects with MTX usage ($\geq$3 months duration, 50.5% of patients). Time-averaged 28-joint Disease Activity Scores (TA-DAS28) were calculated at 12 and 24 weeks. JSN was assessed at week 24. Post hoc analyses evaluated the relationship between TA-DAS28 categories and JSN change (ΔJSN) from baseline to weeks 12 and 24 in the intention-to-treat population.

Results: Mean overall ΔJSN at week 24 was -0.2 for the ADA $\pm$ MTX group and 0.4 for the placebo $\pm$ MTX group ($P < 0.001$). Mean ΔJSN appeared to increase with TA-DAS28 in the placebo group but not the ADA group (Table 1).

Conclusions: JSN was associated with TA-DAS28 in the placebo $\pm$ MTX group, but not the ADA $\pm$ MTX group. These data suggest that ADA may alleviate JSN independent of inflammation, potentially through inhibition of chondrocytic release of matrix-degrading substances.

Disclosure statement: B.G., F.L. and M.O. are employees of Abbott and may own Abbott stock or stock options. R.L. has received research grants and consultancy fees from, and is/has been a member of speakers' bureaus for Abbott, Amgen, Centocor, Pfizer/Wyeth, UCB and Bristol-Myers Squibb. C.R. has received research grants from Abbott, Amgen, Pfizer and Centocor, and consultancy fees from Centocor, Schering-Plough, Bristol-Myers Squibb and Calcimedica.

TABLE 1.

ΔJSN $\pm$ SD (n)	TA-DAS28 Category			
	$\leq$2.6	>2.6-3.2	>3.2-5.1	>5.1
Week 12				
Placebo $\pm$ MTX[a]	0.2 ± 1.16 (9)	0.1 ± 0.17 (9)	0.2 ± 0.7 (79)	1.0 ± 2.52 (52)
ADA $\pm$ MTX[a]	-0.1 ± 0.79 (40)	0.0 ± 0.32 (27)	-0.4 ± 1.49 (59)	0.0 ± 1.01 (15)
P value[b]	0.85	0.59	<0.001	0.02
Week 24				
Placebo $\pm$ MTX[a]	0.2 ± 0.99 (12)	0.0 ± 0.14 (12)	0.1 ± 0.59 (75)	1.1 ± 2.58 (50)
ADA $\pm$ MTX[a]	0.0 ± 0.56 (49)	-0.2 ± 1.22 (26)	-0.4 ± 1.43 (52)	0.2 ± 0.9 (14)
P value[b]	0.77	0.18	0.001	0.14

[a]MTX used by subjects with $\geq$3 months MTX duration before baseline. [b]P value for difference between treatment groups

254. HIGH LEVEL RESPONSES IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GOLIMUMAB: RESULTS FROM WEEK 104 OF THE GO-REVEAL STUDY

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Background: The purpose of this study was to assess high level responses in active psoriatic arthritis pts treated with golimumab (GLM) through wk104.

Methods: PsA pts with $\geq$3 swollen and $\geq$3 tender joints and psoriasis (PsO) were randomized to: subcutaneous (SC) PBO (Grp 1), GLM 50 mg (Grp 2), and GLM 100 mg (Grp 3) q4wks. At wk16, pts with inadequate response entered early escape (EE). Grp 1 crossed over to GLM 50 mg at wk24. In open label extension (OLE), pts could be dose-escalated (DE), from GLM 50 mg to 100 mg. 104wk analyses were based on observed data and randomized grps; no statistical comparisons were done. High level responses were assessed using DAS28 (CRP) score <2.6, PASI90, HAQ<0.5, and proportion of pts without enthesithis, dactylitis or clearing the target fingernail PsO.

Results: 405 pts were randomized: (Grp 1:113pts, Grp 2:146pts, and Grp 3:146pts); at wk104, 335pts (88, 118& 129, respectively) continued treatment. GLM was significantly better than PBO in improving signs and symptoms and radiographic damage at wk24 as previously reported. High level responses through wk 104 are summarized in Table 1. Through wk104, 4.4% (11/248) and 5.3% (12/227) of GLM50mg and 100 mg pts, respectively, discontinued GLM due to AEs, and 6.5% (16/248) and 7.9% (18/227) of GLM50mg and 100 mg pts experienced SAEs. Injection site reactions were mild and occurred in 7.7% (19/248) and 7.0% (16/227) of GLM50mg and 100 mg pts. Histoplasmosis was reported in 1pt (GLM100mg). There were 8 malignancies: 3 GLM 50 mg pts (basal cell, colon, lung small cell), and 5 GLM 100 mg pts (3 basal cell, 1 prostate and 1 small cell lung ca). 1pt died due to lung ca and 1 due to a climbing accident.

Conclusions: Approximately 50% or more of GLM-treated pts treated achieved DAS28 remission or high level improvement in PsO (PASI90) or returned to normal physical function (HAQ$\leq$0.5) after 2yrs of treatment. Approximately 25% of pts achieved simultaneous improvements in those three parameters. Enthesithis and dactylitis resolved in approximately 50% and 80% of pts, respectively. Target nail PsO cleared in more than 50% of pts. Through wk104, GLM demonstrated safety profile similar to that observed for other anti-TNF agents.

Disclosure statement: D.G., A.K., G.K., I.M. and P.M. have received research grants from Centocor Research & Development, Inc. N.G., M.M., S.M., S.X. and J.Z. are employees of Centocor Research & Development, Inc.

TABLE 1.

	Group 1*	Group 2**	Group 3***
Randomized pts	113	146	146
Pts with DAS28<2.6	64.0% (55/86)	64.4% (76/118)	68.0% (87/128)
Pts with PASI90 (among pts with baseline PSO$\geq$3%BSA)	47.7% (42/88)	49.2% (59/120)	51.5% (67/130)
Pts with HAQ $\leq$0.5	51.7% (45/87)	59.2% (71/120)	53.9% (69/128)
Pts with DAS28 <2.6 and PASI90 and HAQ $\leq$0.5	23.3% (20/86)	28.0% (33/118)	28.6% (36/126)
Pts with enthesitis (among pts with enthesitis at baseline)	56.9% (41/72)	43.0% (37/86)	46.0% (46/100)
Pts with dactylitis (among pts with dactylitis at baseline)	7.1% (2/28)	21.4% (9/42)	19.6% (9/46)
Pts with no target finger-nail PSO (among pts with fingernail PSO at baseline)	51.5% (34/66)	56.4% (44/78)	61.7% (58/94)

*includes patients randomized to PBO who switched to GLM 50 mg in EE at week16 or crossed over at week24 and patients who DE from 50 mg to 100 mg in OLE (n=26) **includes patients randomized to GLM 50 mg who remained on 50 mg, EE to 100 mg at week16 or who DE from 50 mg to 100 mg (n=28) in OLE ***includes patients randomized to GLM 100 mg

255. ALLELE-SPECIFIC MEASUREMENT OF MHC PROTEIN TURNOVER IN DENDRITIC CELLS: APPLICATION TO ANKYLOSING SPONDYLITIS

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Background: MHC polymorphisms may confer increased suscept-ibility to autoimmune disease by modulating the intracellular fate of MHC proteins. One example is the association of ankylosing spondylitis (AS) with B27 subtypes that exhibit slow folding in the endoplasmic reticulum and aberrant post-Golgi dimerisation. However, allele-specific differences in MHC class I protein fate have been difficult to evaluate in antigen-presenting cells (APCs) from patients, due to a lack of enabling methodologies.

Methods: Biosynthetic labelling with heavy water (2H2O) and peptide mass spectrometry can be used to quantify protein synthesis in immortalised cell lines (De Riva et al., Anal. Biochem., 2010). This approach was extended here to human peripheral blood monocyte-derived dendritic cells (MoDC) derived from AS patients or from B27-matched or B27-negative healthy donors. Monocytes were differentiated using GMCSF and IL4 and the resultant MoDCs labelled with 5% 2H2O in media for up to 72 hours. Folded HLA-ABC molecules were immunoprecipitated, resolved by SDS-PAGE, and digested with trypsin. HLA class I peptides were identified by LC/MS/MS analysis and compared to each donor's HLA genotype. Mass isotopomer distributions of selected peptides were quantified by LC/MS before and during 2H2O labelling and used to calculate rates of fractional protein synthesis and turnover. As an internal control, HLA-DR molecules were immunoprecipitated and turnover was measured using a monomorphic DR peptide.

Results: Spontaneous MoDC activation varied with cell density, and conditions minimising this effect were established. 2H2O labelling did not activate MoDCs, provided that LPS was excluded. Label incorporation was detectable in monomorphic and allele-specific class I-derived peptides, including B27-specific peptides. Turnover rates of MHC class I molecules in immature MoDC were measured precisely and, in healthy donors, resembled published turnover rates. Whereas class I synthesis persisted after LPS treatment, HLA-DR synthesis and turnover were shut down 24 hours following LPS stimulation. We are now comparing B27 turnover rates with those of other class I molecules and examining MHC protein turnover in patients with AS.

Conclusions: The 2H2O/peptide MS approach permits precise, non-radioactive quantification of MHC class I protein turnover, including B27, in small-scale cultures of MoDC. The ability to perform allele-specific measurements in short-term cultures of antigen-presenting cells from AS patients will be instrumental in dissecting the impact of B27 and other disease-related variables on MHC protein turnover.

Disclosure statement: R.B. is a consultant for KineMed, Inc. and holds stock options. All other authors have declared no conflicts of interest.

256.   MASS SPECTROMETRY-BASED DETECTION AND QUANTITATION OF PUTATIVE BIOMARKERS FOR ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is a common, inflammatory rheumatic disease with a predilection for the axial skeleton, affecting 0.2% of the population. The aetiology of AS is unknown and the diagnosis and prognosis is challenging. Current diagnostic criteria rely on a composite of clinical features and sacroiliac joint radiological changes with a mean time of diagnosis up to 5 years. Our study focuses on the identification of early biological indicators for AS. We have carried out a global comparison of proteins in the blood of AS patients and healthy subjects after depleting the 14 most abundant proteins from serum pools using an antibody based affinity column and alternatively biochemical depletion of immunoglobulins and albumin. The depleted serum was further processed to characterize proteins, endogenous peptides and small metabolic molecules by mass spectrometry. The detected compounds were quantified and, where possible, identified. The initial experiments showed that 44 proteins, 51 endogenous peptides and 42 potential metabolites in serum from AS patients were regulated as compared with healthy controls.

Methods: The detection and identification of proteins, peptides or metabolites in body fluids is complex. The dynamic range of proteins in serum is 12 orders of magnitude and 12 proteins only represent 95% of the protein content. We used the Multiple Affinity Removal System

(MARS, Agilent) to deplete the 14 most abundant proteins in human serum. Proteins were separated from small endogenous peptides and other small molecules by ultrafiltration (5 kDa MWCO). The flow through was enriched for organic molecules by C18 purification while the retentate was digested with trypsin. Both samples were subjected to a LC-MS/MS workflow (Agilent 6520 Q-Tof with Chip-MS) in triplicates. The label-free data was analysed using Progenesis LC-MS software (nonlinear Dynamics). Alternatively we biochemically depleted serum pools of immunoglobins and albumin and used Tandem Mass Tags (TMT, Thermo) to differentially label control and AS serum pools before fractionating the combined peptide samples by preparative isoelectric focussing and LC-MS/MS analysis.

Results: Both experimental setups led to the identification of proteins which are regulated in AS patient serum pools. In the label-free approach, we identified 13 proteins which are regulated in AS patient serum by at least 2-fold, while the TMT based quantitation of the serum proteome identified 33 regulated proteins. Furthermore, we found 51 differentially regulated endogenous peptides and 42 potential metabolites.

Conclusions: Here we present an approach to assess differences in patient sera using state-of-the-art proteomic technology. The discovery of differentially regulated proteomic and metabolic com-pounds in patient serum by mass spectrometry will provide the framework for identifying potential biomarker candidates in Ankylosing Spondylitis.

Disclosure statement: The authors have declared no conflicts of interest.

257.   LOW-DOSE INFLIXIMAB TREATMENT FOR ANKYLOSING SPONDYLITIS: FIVE YEAR FOLLOW-UP

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Background: The licensed and recommended dose of infliximab for the management of Ankylosing Spondylitis (AS) is 5 mg/kg every 6-8 weeks. There is evidence that the lower dose of 3 mg/kg has efficacy in AS. We previously reported a series of 22 consecutive AS patients treated between 2002 and 2004 with low dose infliximab at a dose of 3 mg/kg 8 weekly. After 12 months of follow up, 63% (n = 14) of these patients had achieved and maintained a 50% BASDAI response. We now report the follow up for these patients after a further 5 years.

Methods: The 14 AS patients (having initially fulfilled the New York criteria) who remained on low dose infliximab continued to be followed up in a specialised biologic clinic on a routine basis. Data on clinical assessments, drug treatment, metrology, and laboratory tests were collated on a departmental database. In the case of loss of efficacy, the dose of infliximab was increased or the anti TNF agent was switched, as per departmental protocol. If efficacy was waning before the time of the next infusion, then the low dose was maintained but frequency of infusions was increased. Conversely, dosing intervals were increased for patients who remained in remission. Direct drug cost savings after using the low dose infliximab regimen were estimated.

Results: In 2010, 9 of 14 patients are still successfully being treated with low dose infliximab, at a median frequency of 7 (6-12) weekly infusions. The median duration of infliximab treatment for these 9 patients is 80 (60-99) months. (1 patient had an 18 month gap in treatment as he was in remission). 33% are on concomitant DMARDs and 66% are prescribed as required anti-inflammatory medication. The median BASDAI for this cohort at last assessment was 1.135 (0-3.4) and median BASFI 1.29 (0-4.62). Of the other 5 patients, the median survival on low dose infliximab was 30 months. 2 patients improved on 5 mg/kg infliximab and the other 3 had a good clinical response when switched to subcutaneous anti TNF therapy. The cost of each 100 mg of infliximab was taken as £419.62 (cost as per British National Formulary, September 2010).The current body weight of the 9 patients was used to estimate doses of infliximab given over the median treatment period of 80 months. Using the median dosing frequency of 7 weekly infusions, the cost of infliximab 3 mg/kg for these 9 patients would be £448, 873.60 over 80 months. This is in comparison to the cost of giving 5 mg/kg at the licensed dose over the same period- every 6 weeks-£872, 809.60 or every 8 weeks-£654,607.20. Therefore, using the median results to estimate, the low dose infliximab saved the department between £2-400,000 over the past 5 years.

Conclusions: Of the original cohort of 22 patients treated with low dose infliximab, 9 (41%) maintained a BASDAI 50 response over 5-8

years of follow up. Starting at a low dose of infliximab for AS and then titrating up to the licensed dose, if required, appears to have clinical efficacy and significant economic benefit.

Disclosure statement: The authors have declared no conflicts of interest.

258. GOLIMUMAB INHIBITS PROGRESSION OF RADIOGRAPHIC DAMAGE IN PATIENTS WITH PSORIATIC ARTHRITIS: 52 WEEK RESULTS FROM THE GO-REVEAL STUDY

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Background: Golimumab (GLM), a new human monoclonal anti-TNFα antibody demonstrated efficacy in improving articular and dermatologic manifestation, functional status, and quality of life in pts with psoriatic arthritis (PsA). The effect of GLM on the progression of structural damage in PsA pts is being reported now.
Methods: Adult PsA pts with $\geq$3 swollen & $\geq$3 tender joints were randomized to receive SC placebo (PBO) or GLM (50 or 100 mg) q4 wks. At wk16, pts with <10% improvement in swollen and tender joint counts entered early escape (EE) in a double-blinded manner to GLM 50 mg (PBO pts) or GLM 100 mg (GLM 50 mg pts). All pts randomized to PBO received GLM 50 mg from wk24 through wk52. Radiographs of the hands and feet were obtained at wk0, wk24, and wk52. Erosions (ERO) and joint space narrowing (JSN) were evaluated by two independent readers unaware of treatment and image time sequence using the van der Heijde-Sharp (vdH-S) method modified for PsA. Changes from baseline in the modified vdH-S scores were compared at wk 24 using ANOVA with pts' baseline MTX usage (Y/N) as a factor in the model based on the van der Waerden normal score (primary endpoint). Wk24 comparisons were between GLM grps and the PBO grp, based on the original randomized grps even for pts who entered EE at wk16. Missing data was imputed using median change from baseline in total vdH-S scores of all pts within the same MTX stratum or by linear extrapolation. Due to lack of adequate control arm, no statistical comparisons were performed at Wk52.
Results: 405 pts were enrolled. Mean age was 46-48 yrs, median swollen/tender joint counts were 12-14/22-24, HAQ scores were 1.0-1.1, CRP levels were 0.6 mg/dL, and total vdH-S scores were 9.00-10.50. At wk24, the GLM 50mg treatment grp had significantly less radiographic damage than PBO, as measured by the mean change from baseline in total vdH-S score (-0.16 $\pm$ 1.31 vdHS vs 0.27 $\pm$ 1.26 vdHS, respectively). Significantly more GLM -treated pts (50 mg and 100 mg) had no progression defined as change in total vdH-S score $\leq$ 0 compared with PBO-treated pts (78.8% and 76.6% vs 62.7%, respectively). In a subset of pts without ERO or JSN at baseline, significantly more GLM 50 mg and 100 mg pts maintained an ERO and JSN free state. GLM 50 mg and 100 mg randomized pts had less progression at wk52 (mean change from baseline in total vdH-S score [$\pm$SD]: -0.22 ± 1.64 and -0.14 ± 1.53, respectively)as compared with pts randomized to PBO (0.22 $\pm$ 1.38) who began treatment with GLM at wk16/24.
Conclusions: GLM 50mg and 100 mg demonstrated inhibition of structural damage in pts with active PsA through wk24 with the maintenance of this benefit through wk52.
Disclosure statement: A.Ba., A.Be, M.R., W.X. and J.Z. are employees of Centocor Research & Development, Inc. C.C., D.G., A.K., G.K., I.M., P.M. and D.V. have received research grants from Centocor Research & Development, Inc.

259. DIFFERENTIAL RESPONSES TO IL-23 AND ACTIVATED ALLOGENEIC DENDRITIC CELLS IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

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Background: Psoriasis (Ps) is a common inflammatory disease of the skin affecting 1-3% of the population, and is complicated in 15-30% of cases by arthritis (PsA). Genome-wide association studies have identified the IL-23 subunits, p40 and p19, in addition to the IL-23 receptor, as important genes associated with Ps and PsA. IL-23 aids the survival and expansion of Th17 cells and induces T cells to release IL-22. We have recently confirmed that higher proportions of CD4+IL-17+ and CD4+IL-22+ cells are observed in PBMC derived from patients with Ps and PsA when compared with healthy donors (HD). This also corresponded to higher levels of IL-17 and IL-22 cytokine release.
Methods: PBMC derived from HD, Ps, or PsA were stimulated with anti-CD3/anti-CD28 human T activator beads in the presence or absence of 10 ng/ml rhIL-23; supernatants were harvested and analysed by ELISA for IL-17, IL-22 or IFN-γ. Alternatively, cells were stimulated with allogeneic dendritic cells (DC) previously cultured in either medium alone, or PRR agonists including LPS (TLR4), PIC (TLR3), PIC+CLO (TLR3+7), or curdlan (dectin-1).
Results: As expected, cells from patients with either Ps or PsA produced higher levels of both IL-17 and IL-22 when compared to HD cells. IL-23 potentiated secretion of IL-17 but not IL-22 or IFN-γ; this effect was most marked in the Ps and PsA groups. IL-23 release from DC was reproducibly higher following stimulation with PIC + CLO as compared to ultrapure LPS; nevertheless LPS-activated DC were potent stimulators of both IL-17 and IL-22 in an allogeneic mixed lymphocyte reaction, when compared to DC activated with PIC+CLO. Thus stimulation of production of these cytokines did simply not correlate with IL-23 production by DC.
Conclusions: IL-23 is considered an important therapeutic target in Ps and PsA. We demonstrate that IL-23 modulates Th17 cytokine responses in patients with Ps and PsA. In addition IL-17 and IL-22 secretion by T cells could also be up-regulated in an IL-23-independent fashion. This mechanism requires further investigation and may reveal additional therapeutic targets.
Disclosure statement: The authors have declared no conflicts of interest.

260. THE PREVALENCE OF INFLAMMATORY RHEUMATIC DISORDERS AMONG A COHORT OF HIV-INFECTED PATIENTS WITH MUSCULOSKELETAL SYMPTOMS: AN EPIDEMIOLOGICAL STUDY

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Background: Human Immunodeficiency virus (HIV) is a pandemic with an estimated 34 million infected worldwide. Since the advent of anti-retroviral therapies (cART) the prognosis has been transformed resulting in a growing population of HIV-infected patients. However, it is increasingly clear that cART is associated with non-AIDS morbidities. Inflammatory rheumatic diseases have been reported in HIV-infected patients since 1987 although it is unknown if the virus increases the risk of these conditions. We undertook an observational study among a well-characterised cohort of HIV-infected patients attending one clinic, all assessed by one Consultant according to standardised classification criteria in order to quantify prevalence and evaluate impact and response to treatment.
Methods: Between 2005 - 2009, 1600 outpatients were registered in the database of the Department of HIV/GU Medicine with prevalent HIV infection at one large Teaching Hospital NHS Trust in the South East of England. During that period, 295 subjects (18.43%) developed musculoskeletal symptoms or signs and were all referred to a specialist HIV Rheumatology service, where they were assessed by one Rheumatologist. In each case, a history and examination and relevant investigations were carried out. Here we present a detailed review of the clinical features of all subjects with possible or probable inflammatory rheumatic syndromes referent to standardised validated International classification criteria.
Results: Amongst 295 subjects assessed in the HIV Rheumatology clinic, 35 (12.2%) fulfilled diagnostic criteria for a diagnosis of an inflammatory rheumatic syndrome. The most prevalent conditions

were seronegative oligo- or polyarthritis (with axial involvement, 15 cases, prevalence 5%) (without axial involvement, 8 cases, 2.7%). 8 patients fulfilled criteria for a connective tissue disorder (2.7%). Three subjects presented with a symmetrical polyarthritis predominantly affecting hands, feet and knees associated with low titres of rheumatoid factor and negative anti-CCP antibodies. One subject had immune reconstitution Adult-Onset Still's Disease.

Sulphasalazine, hydroxychloroquine and oral prednisolone were effective in HIV infected patients. Limited experience with methotrexate, mycophenolate mofetil and biologics shows evidence of reasonable safety and effectiveness.

Conclusions: The number of people with prevalent HIV infection is growing steadily. As with other studies, we have demonstrated that it is seronegative spondyloarthopathy and seronegative polyarthritis (Reiter's, psoriatic) that predominate in HIV infected patients. However, we have also seen a low prevalence of rheumatoid arthritis and some connective tissue disorders. Management with DMARDS and Biologics is tricky on the background of immunosuppression. Glucocorticoids can be potentiated significantly by concomitant Ritonavir, a common component of most cART regimens.

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261.   INVESTIGATING THE USE OF THE CASPAR CRITERIA IN EARLY PSORIATIC ARTHRITIS

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Background: The classification of psoriatic arthritis (CASPAR) criteria were derived from a large patient dataset and are valid in classifying established PsA (sensitivity 91.4%, specificity 98.7%). However in the original study, only 5% of the cohort had early disease (<12 months disease duration). The aim of this study was to assess the sensitivity and specificity of the CASPAR criteria in classifying early PsA and to compare the results to that of the Moll & Wright criteria.

Methods: The CASPAR criteria were applied to cases of early PsA (<24 months symptom duration) and controls with other forms of early inflammatory arthritis who were all disease-modifying anti-rheumatic drug naive. Gold standard diagnosis was confirmed by a consultant rheumatologist. Proportions of cases and controls meeting the criteria were compared using McNemars test. Receiver operator characteristic (ROC) curve analysis was performed to identify the area under the curve (AUC) and optimal cut point in the CASPAR criteria for a diagnosis of early PsA.

Results: 111 early PsA cases and 111 early arthritis controls (RA n = 82, undifferentiated arthritis n = 13, spondyloarthritis n = 9, inflamm OA n = 4, crystal arthritis n = 3) were recruited. The sensitivity of the CASPAR criteria (score ≥3) in classifying early PsA was 87.4% compared to 80.2% for the Moll and Wright criteria. The specificity for both was 99.1%, with only 1 control patient fulfilling both criteria. The AUC for the CASPAR criteria was 0.991 compared to 0.896 for Moll & Wright. When considering different cut-points for the CASPAR criteria, the best cut-point for classification remained a score of ≥3 as in the original CASPAR analysis. Considering a score of ≥2 gave a higher sensitivity of 99.1% but resulted in a drop in specificity to 94.6%.

When considering the individual components of the CASPAR criteria, 96.4% of cases had current, previous or a family history of psoriasis with 84% having current psoriasis. Dactylitis and nail psoriasis were highly discriminatory as only 1 control patient each had these features. Regression analysis identified that psoriasis and a negative RF were the most important features to differentiate PsA, followed by nail psoriasis and the presence of dactylitis.

Conclusions: The CASPAR criteria are more sensitive than the Moll & Wright criteria in classifying early PsA. Although the sensitivity is slightly lower than that in established disease, the CASPAR criteria are valid for use as inclusion criteria for early psoriatic arthritis trials.

Disclosure statement: The authors have declared no conflicts of interest.

TABLE 1.

CASPAR features of PsA	Cases (n = 111)	Controls (n = 111)
current psoriasis	93	4
previous psoriasis	7	1
family history of psoriasis	20	9
nail psoriasis	42	1
negative RF	107	52
dactylitis	31	1
new bone formation	2	0

262.   PREDICTION OF EARLY RESPONSE TO ANTI-TNF THERAPY AND DISEASE ACTIVITY STATE USING THE ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE

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Background: We previously reported that in the ASSERT and GO-RAISE studies, BASDAI50 response can be accurately predicted with a combination of baseline characteristics. This analysis compares the accuracy of predicted response rates and disease activity as measured by different assessments, including the ankylosing spondylitis disease activity score (ASDAS).

Methods: The ASSERT and GO-RAISE trial data were combined and baseline characteristics were used to predict the probability of achieving week 12 ASAS20, BASDAI50 and ASDAS major response and BASDAI and ASDAS scores at week 12. Univariate analyses identified baseline predictors for response. Variable associations were explored using Spearman correlation analysis. A stepwise selection procedure using logistic regression, ROC and correlation analyses was used to select a final set of predictors. Logistic regression was used to calculate the predicted week 12 BASDAI and ASDAS scores and the probability of week 12 response to anti-TNF or placebo respective to combined selected predictors at baseline. The accuracy of prediction between the different assessments was compared using ROC analyses and R-square.

Results: 479 AS patients (NY modified criteria) treated with anti-TNF and 156 patients treated with placebo with continued conventional therapy, with BASDAI and spinal pain assessment ≥ 4 were included. Age (mean 39.5; SD 11.3 yrs), BASFI, (mean 5.4; SD 2.2 cm), Berlin enthesitis-score (mean 2.4; SD 2.9), therapy (anti-TNF or placebo), CRP (mean 2.1; SD 2.4 mg/dL) and HLA-B27 genotype [(+) or (-)] were retained as final predictors of response. The area under the ROC curve of the model which included the six selected predictors (log transfer of CRP values) and interactions between predictors was 0.85, 0.79, and 0.75 and the R-square was 0.43, 0.33, and 0.24 for week 12 ASDAS major response, BASDAI50 response and ASAS20 response, respectively. This indicates good accuracy for prediction of BASDAI50 and ASDAS major response and fair accuracy for ASAS20 response. The R-squares of 0.49 and 0.27 for ASDAS and BASDAI scores respectively, indicate that the week 12 disease activity measured by ASDAS could be more reliably predicted.

Conclusions: Elevated CRP, lower age, lower enthesitis score, lower BASFI, and presence of HLA-B27 genotype are associated with a better treatment response at week 12 in ASSERT and GO-RAISE. The values of these characteristics at baseline allow calculating the predicted response rates and future disease activity of an individual patient. The accuracy of predicting ASDAS and ASDAS response is good and higher than that of other assessments.

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263.   EARLY REFERRAL OF ANKYLOSING SPONDYLITIS PATIENTS: RESULTS OF ONE YEAR OUTCOME OF A SPECIALIZED EARLY ANKYLOSING SPONDYLITIS CLINIC

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Background: Objective: Development of a protocol to be applied through a specialized Early Ankylosing Spondylitis Clinic (EAS clinic) that is able to discriminate between different categories of Low Back Pain (LBP) for the sake of shortening the time taken to reach the correct diagnosis and providing the appropriate treatment.

Methods: 42 patients with possible inflammatory LBP were assessed over 12 months in a special EAS clinic. The patients' selection criteria were: symptoms of inflammatory LBP (>3 months), age <40 years, insidious onset, morning stiffness >30 min, no improvement with rest and pain at night with gradual improvement upon getting up or with exercise. Each patient completed a copy of the multidimensional PROM questionnaire for spondyloarthritis [1]. Clinical assessment was carried out for: arthritis, enthesitis, uveitis, dactylitis, nail changes, psoriasis, inflammatory bowel disease (IBD), response to NSAIDs and family history for spondyloarthritis. Basic blood testing was carried out including ESR, CRP and HLA-B27. X-ray was done for every patient to asses for sacroiliitis (according to modified NY criteria) as well as spondylitic changes. MRI scan for the dorso-lumbar spine and sacroiliac joints to assess for active inflammatory changes and the presence of any other focal pathology was also requested.

Results: The mean age of the whole sample was $32.2 +/- 3.8$ years. 78.6% (33/42 patients) were males with a mean disease duration of $14.4 +/- 2.2$ months (range: 6months-6 years). 28 patients were diagnosed to have spondyloarthritis (5 Ankylosing spondylitis, 8 IBD, 15 psoriasis). The remaining 14 patients had other causes for LBP (8 with L5/S1 disc bulge, 6 partial sacralization of L5/ mechanical LBP). 18/42 (43%) of the patients had HLA-B27 positive. Chest expansion mean was $4.1 +/- 0.2$ cm), modified Schober's test was 15-17.5 ($+/-$ 0.61 cm). In the AS group of patients ESR and CRP were negative predictors for MRI findings ($p >0.05$). HLA-B27 prevalence was higher, but not significant, in the spondylitis group of patients. Spondylitis and active sacroiliitis were reported in 18/28 patients MRI scans. Sensitivity of the referral model was 77.4% whereas specificity was 79.3% (specificity was higher with image modoality 96.3%).

Conclusions: Application of this model has helped in identifying the patients suffering from early forms of the disease. Patients with chronic LBP (>3 m) with the onset of symptoms at an age <45 years should be proposed to physicians in primary care to screen the patients for possible axial spondylitis. The likelihood of spondylitis increases if other screening parameters were present, suggesting that this is a group of patients who should be referred to the rheumatologists with higher priority. L5/S1 disc bulges remain a strong differential diagnosis for sacroiliitis and should be excluded first.

Disclosure statement: The authors have declared no conflicts of interest.

Reference

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264.   HD6: A NOVEL MONOCLONAL ANTIBODY THAT RECOGNISES A SUBSET OF HLA-B27 MOLECULES STRONGLY IMPLICATED IN SPONDYLOARTHRITIS DISEASE PATHOGENESIS

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Background: Possession of HLA-B27 is strongly associated with development of the spondyloarthropathies, yet the mechanism by which HLA-B27 confers this susceptibility is unclear. HLA-B27 forms both heterotrimers (B27HT) associated with peptide and β2m, and heavy chain homodimers (B272). It has previously been shown that B272 can assemble from unstable B27HT undergoing endosomal

recycling from the surface. A pathogenic role for these homodimers has been proposed. However, determination of the extent, distribution and triggers of B272 expression have been hampered by the lack of a specific detection reagent. In order to investigate the role of homodimers in AS, we generated an antibody to B272 using phage display technology. Here, the recognition of HLA-B27 by this novel mAb is characterised.

Methods: Phage display technology was used to generate monoclonal antibodies specific for B272. Biotinylated recombinant B27HT and B272 complexes were used for selection of a phage fAb library. One selected clone, HD6, was then sub-cloned to generate a chimeric antibody comprising human fAb2 and murine IgG1 Fc. ELISA was used to confirm its specificity for B272 complexes. For recognition of cell-expressed B272, human B cell line transfectants, AS patient and control PBMCs, and splenocytes isolated from HLA-B27 transgenic rats were used and results analysed by FACS. For further characterisation of the epitope, transfectants were i) treated with acid, ii) cultured with HLA-B27 specific or control peptides or iii) treated with the protease papain prior to FACS analysis.

Results: 1) In ELISA, HD6 specifically recognised recombinant B272 but not HLA-A2, B7 or B27HT. 2) HD6 recognises a novel subset of B27 molecules on the surface of transfected B cell lines, including LBL721.220, C1R and T2 transfectants. 3) HD6 surface reactivity is dependent on level of B27 surface expression and is inhibited by a C-terminal HA tag. 4) The HD6 epitope is resistant to acid treatment but sensitive to papain cleavage. 5) Peptide addition abrogates HD6 reactivity at the surface for up to 24 h. 6) HD6 bound in FACS to PBMCs from AS patients but not controls, and to a number of cell subsets from splenocytes taken from HLA-B27 transgenic rats but not WT.

Conclusions: HD6 is a novel phage display-derived mAb that recognises both recombinant B272 and an epitope on the surface of HLA-B27 transfected cell lines. HD6 stains monocytes from AS patients, implicating these cells in AS pathogenesis, and a number of cell subsets including monocytes from HLA-B27 transgenic rats. Our data suggest that peptide binding is not necessary for expression of the HD6 epitope, and are consistent with B272 expression and recognition at the cell surface. HD6 will be a powerful tool to address the potential pathogenic role of B272 in SpA and may additionally have therapeutic potential.

Disclosure statement: The authors have declared no conflicts of interest.

Vasculitis

265.   CRYOGLOBULINEMIC VASCULITIS SECONDARY TO HEPATITIS C INFECTION: IS PREDICTION OF DISEASE SEVERITY FEASIBLE?

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Background: Chronic Hepatitis C virus (HCV) infection can sometimes be causative of vasculitis. We assessed the incidence, clinical spectrum and management of cryoglobulinemic vasculitis (CGV) secondary to HCV infection in a tertiary teaching hospital.

Methods: We included 246 consecutive patients with chronic HCV infection admitted to our hospital between 01/01/2004 and 31/12/2008. In those with cryoglobulinemic vasculitis we assessed the duration of infection (more or less than 36 months), clinical features, biologic, immunologic and inflammatory status (estimated GFR - MDRD, complement level, ESR, CRP), viral load, Histological Activity Index (HAI) and disease activity (assessed with the Birmingham Vasculitis Activity Score (VAS) 2003; severe vasculitis was defined as VAS>12).

Results: Of the 246 chronic HCV infection patients, 16 had CGV; 9 had a duration of the disease >36 months (mean duration 37.4 months, SD ± 11, range $= 7$-68 months). Eleven of all the 16 patients had cutaneous involvement, 12 neurologic involvement, 7 renal dysfunction, 4 joint involvement and 1 antiphospholipid syndrome. In 12 (75%) patients ESR was > 25 mm/h, 11 (69%) had abnormal levels of CRP and 6 (38%) had low complement levels. The HAI was > 9 in 12 patients, and the mean VAS2003 was 12 (SD ± 2; range $= 6$-21) Severe vasculitis was associated with duration of infection > 36 months ($p = .03$; $r = .55$), renal involvement ($p = .036$; $r = .83$), lower levels of complement ($p = .044$; $r = .78$) and viral load < 800.000 IU/ml ($p = .041$;