Table 1. Interval between baseline BMD testing and the development of osteoporosis

Baseline BMD	Mean interval to develop osteoporosis (year)		Mean interval to develop osteoporosis in 10% of each group (year)	
	Lumbar spine	Femur neck	Lumbar spine	Femur neck
Normal	9.4 (9.29–9.49)[a]	9.4 (9.25–9.53)[a]	>10	>10
Mild osteopenia	9.2 (8.58–9.71)[a]	9.1 (8.94–9.22)[a]	4.3	>10
Moderate osteopenia	7.9 (6.94–8.76)[a]	9.4 (8.93–9.87)[a]	2.5	7.5
Advanced osteopenia	5.4 (4.61–6.21)[a]	8.6 (7.68–9.50)[a]	1.5	2.2

BMD, bone mineral density. [a]Mean (95% confidence interval).

patients, 4 years in mild, 2 years in moderate, and 1 year in advanced osteopenic RA patients on the basis of L-spine BMD.

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SAT0138 OPTIMIZING TARGETED THERAPY: CAN PROMS FILL THE GAP BETWEEN PATIENTS- AND PHYSICIAN- PERCEIVED REMISSION IN RHEUMATOID ARTHRITIS

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Objectives: 1. To compare the patient perspective on remission in RA in comparison to the rheumatologist perceived remission perspectives.
2. To determine the value of Patient Reported outcomes in identifying specific symptoms and aspects of disease able to define remission in RA from the patient perspective.
Methods: RA patients diagnosed according to ACR/EULAR criteria were treated according to treat-to-target regime with regular disease activity monitoring (every 1–3months). Remission was measured in two ways: 1) patient perceived remission using the question "Would you say that, at this moment, your disease activity is as good as gone? (yes/no)"; and 2) Physician perceived remission was defined as a physician global assessment ≤1 on a 0–10 VAS, phrased: "How active do you think the rheumatoid arthritis of your patient is today?" The study included 188 RA patients (76 males, 112 females; mean age 52.4±11 years) and 87 rheumatologists (30 males, 57 females; mean age 48.7±11.7 years). All participants were asked to complete a questionnaire which was composed of all domains identified in relation to the disease remission. 10 cm visual analogue scale (scored 0–10) was used to illustrate the importance of each factor in an individual opinion. The list included joint pain, functional ability, quality of life, absence of morning stiffness, absence of fatigue, normal laboratory tests, no comorbidity risk, radiologic remission, Disease Activity score and ability to work. In addition, patients were asked to complete a copy of the PROMs [1]. One-way analysis of variance was used for the comparison of independent variables. Spearman correlation coefficient was used to assess the correlation between variables.
Results: There were no significant differences in questionnaire answers in relation to patients' demographics and present disease activity. Regarding the patient perceived remission, the top 4 were: pain (76%), functional ability (71%), quality of life (69%) and fatigue (43%). Regarding the physician perceived remission, the following factors were rated more relevant by rheumatologists than the patients ($p<0.001$): low disease activity score (88%), radiologic remission and progression of erosions (76%), lab measures (ESR/CRP) (57%) followed by difficulties in performing paid work (49%).
Functional ability was scored significantly higher in patients >65 as compared with patients <65 years of age (9.6 vs 8.1 on VAS, p=0.03). In contrast the patient's cohort <65 years of age, rated quality of life at a higher level (9.7) than those below 65 (8.4). Functional ability was scored higher in patients with longer-standing disease as compared to patients with shorter disease duration ($p<0.05$). PROMs enabled the patient and the treating physician identify the aspects of relevance necessary for optimal clinical management.
Conclusions: Different factors are important for rheumatologists and RA patients regarding disease remission. Treatment satisfaction is determined not only by disease activity indices but also by other patient-oriented factors. PROMs could optimise targeted therapy as it can play a significant role in identifying disease activity parameters relevant to both the treating rheumatologist as well as the patient.

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SAT0139 ASSESSING ENTHESITIS BY ULTRASONOGRAPHY IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: In patients with seronegative rheumatoid arthritis (RA) there is a difficulty to make the differential diagnosis with the spondyloarthropathies.
Objectives: To assess the presence of enthesitis in patients with seronegative rheumatoid arthritis in comparison with the healthy controls, patients with seropositive rheumatoid arthritis and ankylosing spondylitis.
Methods: In this cross-sectional study, seronegative and seropositive rheumatoid arthritis patients, who fulfilled the 2010 ACR/EULAR criteria, patients with ankylosing spondylitis and healthy controls have been assessed by grey scale and power doppler ultrasonography for the presence of enthesopathy at the achilles, plantar fascia, proximal patella, distal patella, quadriceps, tibialis anterior, triceps, common flexor and extensor tendons. Clinical assessment of the patient groups included demographic findings, health assessment questionnaire and disease activity score.
Results: In our study, we recruited age and sex matched 27 seronegative RA, 17 healthy controls, 20 seropositive RA and 12 ankylosing spondylitis patients. We evaluated and analysed both right and left sides of the enthesis regions separately which have been indicated in the methods section. The mean DAS28, mean ESR and mean CRP of the patients with seronegative RA were 3.6±1.28, 32.2±21.2 and 12.37±27.77 respectively (Table 1).
Median of Madrid sonographic enthesitis index (MASEI) was 5 in patients with seronegative RA. 4 patients have severe scores. There were significant differences between seronegative RA and healthy controls (3, p=0.014) but no differences has been observed between seronegative RA with seropositive RA (6) and anklosing spondylitis (7) in MASEI scores.
In comparison, hypoechogenicity of quadriceps tendon (16 (29.6%) vs 1 (2.5%), p=0.001), bone erosion at the quadriceps tendon attachment (9 (16.6%) vs 0, p=0.007), hypoechogenicity of triseps (13 (24%) vs 7 (17.5%), p=0.049) have been observed more frequently in patients with seronegative RA than seropositive RA. Significantly higher number of patients with bone erosion at the distal patella (10 (41.6%) v 3 (5.5%), p= <0.001), enthesophyte of achilles tendon (7 (29.1%) vs 2 (3.7%), p=0.001) have been detected enthesophyte of proximal patella (7 (29.1%) vs 0, p≤0.001) in patients with ankylosing spondylitis than seronegative RA.

Table 1

	Seronegative RA	Healthy controls	Seropositive RA	Ankylosing spondylitis
Age, years	51,85±11,49	44,42±7,6	52,05±11,26	41,75±5,1
Women, n (%)	48 (88,9)	34 (100)	36 (90)	20 (83)
RA duration, year	9,8±6,75		11,25±9,1	
RF titre (median)	10,77±3,21		345,88±405,32	12,1±3,23
Anti-CCP titre, median	3,99±4,13		326, 81±286, 2	4,32±3,7
DAS28, median	3,6±1,28		3,73±1,45	
ESR, median	32,2±21,2	23,3±11,8	41,63±28,07	19,83±9,38
CRP, median	12,37±27,77	3,14±3,87	14,34±19,97	6,61±5,6

Conclusions: We observed that enthesis involvement was not seldom in patients with seronegative RA. Furthermore there were also similar frequency of entesis involvement in seropositive patients with RA. The value of enthesis sites evaluationfor the differential diagnosis of patients with seronegative RA should be further investigated and the assessment of enthesis sites in seronegative and seropositive RA patients can be important to detect active and chronic changes at the enthesis region.

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Rheumatoid arthritis - anti-TNF therapy

SAT0140 EFFECT OF OBESITY IN RESPONSE TO BIOLOGICS IN RHEUMATOID ARTHRITIS

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Background: Obesity epidemic has impacted practically every area of health including care of patients with RA. Adipose tissue is an active organ that produces pro-inflammatory molecules. A significant treatment challenge remains is the standard dose of RA medications may not attain same concentrations at sites of inflammation in obese vs non-obese patients thus making them less effective.
Objectives: The study aim was to determine whether obesity represents a risk factor for a poor remission in RA requiring biologic therapies. Obesity may be associated with more severe and refractory inflammation through increased levels of inflammatory adipocytokines leptin, resistin or visfatin or decreased levels of the anti-inflammatory adipocytokine adiponectin. We retrospectively analysed 178 patients diagnosed with RA at East Kent University Hospitals.
Methods: Data analysed for age, sex, disease duration, prior DMARD, positivity RF and anti-CCP antibodies and response to biologics DAS28 score pre-treatment and at 6 months were analysed.Main aim was to analyse any difference between obese and non-obese patients in terms of their response to treatment. Obese patients were defined with a BMI of 30 or above.
Results: See Table 1.

Table 1. Demographics and Baseline Characteristics

Variable	Category	Non-Obese (n=95)	Obese (n=83)	P-value
Sex	Female	61 (64%)	66 (80%)	**0.02**
	Male	34 (36%)	17 (20%)	
Age		53±12	50±13	0.08
Duration disease		8 [6, 11]	12 [7, 14]	**<0.001**
Rheumatoid factor	Negative	20 (21%)	60 (72%)	**<0.001**
	RF	12 (13%)	8 (10%)	
	CCP	17 (18%)	0 (0%)	
	RF/CCP	46 (48%)	15 (18%)	
CRP		35 [10, 51]	24 [7, 40]	**0.02**
ESR		37 [14, 59]	28 [17, 45]	0.57
MTX		15.5±9.2	13.5±9.6	0.15
Administration	Infusion	4 (4%)	5 (6%)	0.74
	Subcutaneous	91 (96%)	78 (94%)	
DAS pre-treatment		5.6±0.7	5.4±0.8	0.06

Results suggested that there were significant differences between two groups for sex, duration of disease, RF and CRP. There was also some evidence of difference between groups in terms of their age and pre-treatment DAS28 score but these differences were only of borderline statistical significance. There was smaller proportion of males in the obese group with 20% male compared to 36% of non-obese patients. Obese patients had on average a longer disease duration with a median of 12 years compared to a median of 8 years for the non-obese group. The RF status also varied between groups with a much higher proportion of patients in the negative category for the obese group. CRP values were significantly lower in the obese group with a median of 24 compared to 35 in the non-obese group.

Table 2. EULAR response between obese and non-obese patients

EULAR response	Non-Obese N (%)	Obese N (%)	P-value
No response	9 (9%)	32 (39%)	<0.001
Moderate response	40 (42%)	36 (43%)	
Good response	46 (48%)	15 (18%)	<0.001
	Non-Obese (n=95), Mean ± SD	Obese (n=83), Mean ± SD	
DAS28 post-treatment	3.2±1.0	4.2±1.3	
DAS28 reduction	2.4±1.3	1.1±1.3	

Non-obese had the best response with 48% good response compared to18% of the non-obese group with post treatment mean DAS28 score of 3.2 and mean reduction of 2.4.

Conclusions: Obesity is important factor that impacts treatment and outcome in RA. Future clinical studies to elucidate the pharmacokinetics of specific biologic agents in relation to BMI should provide further clinical guidance.

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SAT0141 OPTIMAL CIRCULATING ADALIMUMAB LEVELS RANGE ASSOCIATED WITH GOOD CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: TNF inhibitors have become an important part of healthcare worldwide for inflammatory diseases such as RA[1]. Many publications show that responding patients have higher Adalimumab (Ada) serum trough levels (ATL) than non-responders. These factors are influenced by age, weight, gender or pharmacokinetics, which in turn depend on immunogenicity. Concomitant use of immunomodulators such as methotrexate (MTX) reduces immunogenicity and enhances therapy benefits[1,3].Increasing drug dosage in patients with less response is the standard practice, while lowering dosage is advisable in patients achieving remission. Many recent publications[2] assess serum trough levels that reflect optimal response and which could be used as benchmark for guidance to implement the Therapeutic Drug Monitoring.

Objectives: To establish an optimal Ada serum trough level (ATL) range in RA patients associated with good clinical response.

Methods: A prospective observational study with 40 RA patients under Ada treatment recruited in the Rheumatology Unit of Universitary Hospital La Paz was conducted. Demographic data, ATL and clinical activity of patients treated with 40 mg/kg every other week from 4 months up to 12 years of treatment were collected. A total of 206 samples were analyzed [χ=5 (3–13) samples/patient]. Disease activity was assessed using the DAS28 index and clinical improvement with $\triangle$DAS28. ATL were measured with a capture ELISA[3] [correlation with Promonitor (Derio, Vizcaya, Spain) k=1, r=0.91; and with Sanquin (Amsterdam, The Netherlands) k=1, r=0.86] and statistical analysis were performed with GraphPadPrism 5.0 software.

Results: Demographic data of our cohort were: mean age (±SD) 56.75±16.06, with 82.5% of females and 45% of patients treated with concomitant MTX. Sixty-five and 72% of patients were RF and ACPA positive, respectively. ATL were similar in patients treated with concomitant MTX (χ=3.82±2.42 μg/ml) or Ada monotherapy (χ=3.54±2.43 μg/ml) p=0.81.

Consistent with previous studies[1,2], low-disease activity patients (DAS28$\leq$3.2) presented higher Ada circulating levels than patients with high-disease activity [3.7 μg/ml (IQR 2.97–5.48) vs. 1.71 μg/ml (IQR 0.23–4.51), p=0.01]. The median of Ada levels excluding the values (n=6) that showed immunogenicity was 3.42 μg/ml (IQR 1.55–5.03) where 3.50 μg/ml represented the most frequent value (15% of patients). Lack of clinical improvement ($\triangle$DAS$<$1.2) was linked to drug levels below percentile 25 (p=0.04) whilst Ada levels above percentile 75 did not ensure more clinical improvement (p=0.7) than the values around the median.

Conclusions: ATL correlate with the disease activity and with the clinical improvement. The optimal range associated with good therapeutic response after the standard dose is *1.5–5 μg/ml*. Higher circulating drug levels do not entail better response, which indicates they could be unnecessary. The knowledge of the optimal drug ranges can guide the Personalized Drug Therapy in order to maximise effectiveness and minimise costs.

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SAT0142 PREDICTORS OF INADEQUATE RESPONSE AND RAPID RADIOGRAPHIC PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE: A POST HOC ANALYSIS OF 2 RANDOMIZED, CONTROLLED TRIALS OF ADALIMUMAB

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Background: Methotrexate (MTX) is recommended as first-line therapy in patients (pts) with rheumatoid arthritis (RA).[1] However, information is limited regarding factors that may predict a poor response to MTX.

Objectives: To identify predictors of MTX insufficient response (IR) and rapid radiographic progression (RRP) among pts with early RA receiving 6 months (mos) of MTX therapy.

Methods: In OPTIMA, pts with RA $<$1 year were randomized to receive either adalimumab (ADA) 40 mg every other wk (EOW) + MTX weekly (wkly) or placebo (PBO) EOW + MTX wkly for 26 wks. In PREMIER, pts with RA $<$3 years were randomized to receive ADA 40 mg EOW + MTX wkly, ADA 40 mg EOW + PBO wkly, or PBO EOW + MTX wkly for 2 years. This post hoc analysis compared MTX-IR pts, defined as not reaching stable low disease activity at wks 22 and 26 in OPTIMA and wks 20 and 24 in PREMIER, with pts who responded to initial MTX monotherapy. Comparisons were also made between pts who did and did not have RRP, assessed by an increase in modified Total Sharp Score (mTSS) of $>$1.5 from baseline (BL) to 6 mos. In pts with available data, backward logistic regression was used to identify potential predictors of MTX-IR and RRP. Candidate predictors included BL demographics, time-averaged disease parameters for 3 time intervals (through 4 wks, 8 wks, and 12 wks of MTX exposure), and BL disease characteristics for the 12-wk interval. Time-averaged variables were calculated as area under the curve standardized for length of time interval.

Results: This analysis included 525 MTX-IR and 162 MTX responders. Mean disease duration at BL was 6 mo for both groups. The mean Disease Activity Score 28 (C-reactive protein; DAS28[CRP]) was 6.2 vs 5.6, Health Assessment Questionnaire Disability Index (HAQ-DI) was 1.6 vs 1.3, and mTSS was 15.5 vs 12.2 for MTX-IR vs MTX responders, respectively. 171 pts experienced RRP, while 499 pts had no RRP; the mean disease duration at BL was 6 mo for both groups. The mean DAS28(CRP) was 6.4 vs 6.0 and HAQ-DI was 1.6 vs 1.5 for pts experiencing RRP vs pts who did not experience RRP, respectively. Mean mTSS at BL was higher for pts who experienced RRP (20.7) vs those who did not (12.4). Predictors of MTX-IR and RRP at 6 mos are shown in the Figure. Time-averaged HAQ-DI and DAS28(CRP) through 12 wks were the strongest predictors of both MTX-IR and RRP. Additionally, early clinical response (time-averaged DAS28[CRP]) at both 4 and 8 wks was predictive of both MTX-IR and RRP; however, time-averaged HAQ-DI was not predictive until wk 12.

Conclusions: In the OPTIMA and PREMIER trials, post-BL measures of RA activity appeared to be the strongest predictors of subsequent MTX-IR and of RRP. Pts who are likely to progress on MTX or have RRP may be good candidates for switching to earlier step-up therapy to reduce the likelihood of permanent bone damage.

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