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.

References:

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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.

References:

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