SAT0101

ABATACEPT IN RHEUMATOID ARTHRITIS ASSOCIATED-INTERSTITIAL LUNG DISEASE: SHORT TERM OUTCOME AND PROGNOSTIC FACTORS

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Background: The prevalence of interstitial lung disease (ILD) in rheumatoid arthritis (RA) varies in the medical literature from 1% to 67% and is a major cause of mortality. Previous works have identified increased age, smoking and anticytoplasmic protein antibodies (ACPA) titre as risk factors for RA-ILD (RA-ILD). Conventional treatments for RA may lead to a new onset or worsening of RA-ILD, so treatment should be identified to prevent the onset or exacerbation of RA-ILD. Studies have shown that abatacept (ABA) may improve the outcome of RA-ILD.

Objectives: The aim of our study is to evaluate ABA effectiveness and safety in patients with RA-ILD.

Methods: We enrolled RA-ILD patients who started treatment with ABA. All patients underwent thoracic high-resolution computed tomography (HRCT) at the beginning of ABA treatment and after 18 months of therapy. HRCT abnormalities were evaluated using a computer-aided method (CaM). At each visit clinical, laboratory and respiratory function characteristics were collected and the Clinical Disease Activity Index (CDAI) and the Health Assessment Questionnaire Disability Index (HAQ-DI) for disease activity and functional disability were measured. The cohort was divided into three groups based on the CaM-HRCT results: patients with a lung fibrosis progression of 15% or more were defined as "worsened"; those with a reduction of 15% or more were defined as "improved"; all other patients were defined as "stable". The 15% threshold of change, derived from the CaM assessment, results from the determination of the standard deviation of the mean value change after 18 months of follow-up of the cohort. The multivariate regression model was used to assess the strength of the association between RA characteristics and HRCT response to ABA.

Results: Forty-four patients (81% women) with a mean age of 59.1±8.0 years and a mean duration of the disease of 7.5±3.1 years were recruited. Twenty-three (52.3%) patients were positive for ACPA and 28 (63.6%) for rheumatoid factor. Five patients (11.4%) showed deterioration of ILD, 31 (70.6%) were in the "stable" group, and 7 patients (16.0%) experienced improvement over a mean follow-up period of 18 months. The factors related to ILD deterioration were use of methotrexate (MTX) ($p=0.0078$), and current smoking habit ($p=0.0054$), according to multivariate regression analysis (Table).

Conclusion: Treatment with ABA is associated with an RA-ILD stability or improvement rate of 86.6% of patients, while the worsening rate is 11.4%. Concomitant treatment with MTX and current smoking habit are factors associated with RA-ILD worsening. MTX discontinuation and smoking cessation should be strongly promoted in patients with RA-ILD.

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Table. Multivariate regression analysis of the variables related to the worsening of RA-ILD

Independent variables	Coefficient	Std. Error	t	P	r partial
(Constant)	1.6370				
Age	-0.0012	0.0050	-0.2	0.8131	-0.042
Sex	0.025	0.1	0.23	0.8161	0.042
Disease duration	0.015	0.017	0.89	0.3799	0.15
ACPA positivity	-0.012	0.071	-0.18	0.8566	-0.032
RF positivity	0.0030	0.079	0.038	0.9694	0.0069
Current smokers	-0.34	0.11	-2.99	0.0054	-0.47
MTX use	-0.39	0.13	-2.84	0.0078	-0.45
DLco	0.0052	0.0061	0.84	0.4030	0.15
FVC	-0.0088	0.0088	-1.006	0.3224	-0.17
CAM-HRCT (% fibrosis)	0.00082	0.0091	0.09	0.9285	0.016
CDAI	-0.0074	0.0038	-1.96	0.0588	-0.33
HAQ-DI	-0.017	0.14	-0.11	0.9059	-0.021

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SAT0102

NONINFLAMMATORY PAIN IS A FREQUENT PHENOMENON IN RHEUMATOID ARTHRITIS AND RESPONDS WELL TO TREATMENT WITH SARILUMAB

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Background: Inflammation is clearly a key driver of pain in rheumatoid arthritis (RA). However, in some patients the level of pain exceeds what would be expected based on the amount of synovitis observed, which may indicate the presence of noninflammatory pain (NIP). Interleukin-6 (IL-6) has been shown in animal models to increase sensitization to pain and may play a role in NIP.

Objectives: To assess the effect of sarilumab, a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA, on NIP and disease activity, stratified by baseline (BL) NIP status.

Methods: The analysis included data from three Phase 3 studies of sarilumab: MOBILITY (NCT01061736), MONARCH (NCT02332590), and TARGET (NCT01709578). Patients received double-blind placebo or sarilumab 150mg or 200mg subcutaneously (SC) every 2 weeks (q2w), plus weekly csDMARD (MOBILITY and TARGET), or adalimumab 40mg or sarilumab 200mg SC q2w as monotherapy (MONARCH).

NIP was defined using an established formula: tender 28-joint count (TJC) – swollen 28-joint count (SJC) ≥ 7 .^{1,2} Patients were assessed for NIP at study BL and for change in NIP status at Weeks 12 and 24. The proportion of patients achieving ACR20/50/70, Clinical Disease Activity Index (CDAI) ≤ 10 , and DAS28-CRP < 3.2 at Week 24 was assessed in patients with and without BL NIP. No inferential statistics were performed.

Results: Of 2112 patients in the analysis, 490 (23%) met the criteria for NIP at study BL: MOBILITY, $n = 294/1197$ (25%); MONARCH, $n = 90/369$ (24%); TARGET, $n = 106/546$ (19%). BL demographics were similar for patients with or without BL NIP: mean age (SD) was 52.6 (10.7) versus 51.2 (12.3) years, and 85% versus 81% were female. Patients with BL NIP had higher CDAI, DAS28-CRP, pain Visual Analog Scale (VAS), and TJC at BL versus patients without NIP (Table). Of patients with NIP at BL, those who received sarilumab were more likely to have no NIP at Weeks 12 and 24 versus patients who received placebo or adalimumab (Figure 1). The percentage of patients achieving improvements in disease activity at Week 24 was greater for sarilumab versus adalimumab among both patients with and without BL NIP, and these differences were larger among patients with BL NIP for all assessments except ACR50 (Figure 2).

Table. Baseline characteristics

Mean (SD)	Patients with TJC – SJC ≥ 7	
	Yes (n = 490)	No (n = 1622)
Duration of RA, years	9.1 (8.6)	9.7 (8.4)
TJC, 0–28	21.7 (4.7)	14.3 (6.2)
SJC, 0–28	10.7 (4.3)	13.1 (6.0)
CRP, mg/L	22.7 (27.0)	22.9 (24.0)
HAQ-DI, 0–3	1.8 (0.6)	1.7 (0.6)
DAS28-CRP	6.4 (0.7)	5.9 (0.9)
CDAI	46.0 (9.4)	40.4 (13.0)
Pain VAS	72.3 (18.2)	67.0 (20.7)

Figure 1 Percentages of patients with baseline noninflammatory pain who had noninflammatory pain at Weeks 12 and 24*

*For MOBILITY and TARGET, data are shown only for patients who received sarilumab 200 mg

Conclusion: NIP was prevalent at BL in the patient populations assessed. Among patients with BL NIP, a lower proportion continued to have NIP at Weeks 12 and

Figure 2 Percentages of sarilumab and adalimumab responders at Week 24 by baseline noninflammatory pain status

24 when treated with sarilumab versus placebo or adalimumab. Patients with and without BL NIP had greater improvements in pain when treated with sarilumab versus adalimumab. The difference in clinical improvement was greater among patients with BL NIP versus without BL NIP for most measures. These trends support the emerging concept that mechanisms other than direct inflammation may contribute to pain in RA, potentially mediated via IL-6 signaling.

References:

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SAT0103

THE EFFECT OF BODYWEIGHT ON RESPONSE TO INTRAVENOUS OR SUBCUTANEOUS TOLICIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tocilizumab is an IL-6 receptor humanised monoclonal antibody treatment option in rheumatoid arthritis (RA) who have not responded or are intolerant of disease modifying anti-rheumatic drugs (DMARDs) or other biologics. Tocilizumab was available initially as an intravenous (IV) preparation, dosed according to weight, and more recently as a subcutaneous (SC) preparation given at 162mg/weekly irrespective of bodyweight.

Obesity is highly prevalent in RA and there has been concern that starting or switching patients to SC tocilizumab could reduce its effectiveness in those patients with a higher body weight when compared to IV tocilizumab.

Objectives: To investigate the relationship between bodyweight and DAS28 response at 6 months in tocilizumab naïve RA patients starting IV or SC tocilizumab.

Methods: The study population comprised RA subjects recruited to the BSRBR-RA up to 30/11/2018 commencing IV or SC tocilizumab for the first time. Patients had

to be tocilizumab naïve and have at least one six monthly study follow-up recorded after starting tocilizumab. Baseline characteristics at point of starting tocilizumab are described. Linear regression, fully adjusted for relevant confounders, was used to investigate the relationship between change in DAS28 score from baseline to six months and body weight per ten kilograms (kg), and in a separate analysis, as BMI category. Multiple imputation was used to handle missing data.

Results: 1241 patients starting tocilizumab (902 IV, 339 SC) were eligible for analysis. The median age was 59 years, majority were female, and had median disease duration of 11 years at baseline. Over seventy percent had prior biologic exposure. Median weight was 77kg for IV and 76kg for SC starters, and the majority of patients were categorised as normal weight (30% IV, 37% SC) or pre-obesity (31% IV & SC) according to BMI. Median DAS28 score was 5.8 (IV) and 5.5 (SC) at start of treatment with median improvement after 6-months of 1.50 and 2.02 units respectively. The fully adjusted linear regression model showed no association between body weight or BMI and change in DAS28 score at six months for patients starting IV or SC tocilizumab. (Table).

Table

Baseline Variable	Intravenous TCZ patients (n=902)	Subcutaneous TCZ patients (n=339)
Age, median (IQR)	58 (50-67)	60 (51-70)
Gender, n (%) female	708 (78)	233 (74)
Disease duration, median (IQR) years	11 (4-21)	11 (4-21)
DAS28 score, median (IQR)	5.8 (5.1-6.6)	5.5 (4.7-6.5)
Change in DAS28 score, median (IQR)	-1.50 (-3.10 - -0.23)	-2.02 (-3.72 - -0.37)
Weight in KGs, median (IQR)	77 (64-91)	76 (64-88)
Body weight per 10kgs*	0.04 (-0.01-0.09)	-0.005 (-0.11-0.10)
BMI category*		
Normal weight	ref	ref
Underweight	-0.41 (-1.27-0.46)	0.08 (-1.62-1.77)
Pre-obesity	-0.26 (-0.57-0.05)	0.02 (-0.44-0.48)
Obesity class I, II & III	-0.03 (-0.35-0.29)	0.08 (-0.40-0.55)

*Fully adjusted for age, gender, disease duration, baseline DAS28 score, baseline HAQ score, co-morbidities, and number of previous biologics

Conclusion: Data from this study show that body weight does not appear to affect initial response to IV or SC tocilizumab. This is reassuring given that patients are likely to be given SC tocilizumab due to ease of administration and reduced hospital costs.

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SAT0104

MAINTENANCE OF SDAI REMISSION AND PATIENT-REPORTED OUTCOMES (PROS) FOLLOWING DOSE DE-ESCALATION OF ABATACEPT IN MTX-NAÏVE, ANTI-CITRULLINATED PROTEIN ANTIBODY (ACPA)+ PATIENTS WITH EARLY RA: RESULTS FROM AVERT-2, A RANDOMISED PHASE IIIB STUDY

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Background: The Phase IIIB Assessing Very Early RA Treatment (AVERT)-2 trial (NCT02504268) evaluated SC abatacept (ABA) + MTX vs ABA placebo (PBO) + MTX in ACPA+ patients (pts) with early, active RA. ¹ Results from the 56-wk induction period (IP) showed a significantly greater proportion of pts treated with ABA + MTX (vs MTX alone) reported clinically meaningful improvements in HAQ-DI, global disease activity and pain, which were sustained at 52 wks. ²

Objectives: To report maintenance of SDAI remission and PROs from the AVERT-2 de-escalation (D-E) period.