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Background: There are limited literature data regarding the characteristics of rheumatoid arthritis (RA) patients treated with biologic DMARD (bDMARD) monotherapy.

Objectives: To evaluate the disease and treatment characteristics of RA patients treated with bDMARD monotherapy.

Methods: Multicenter, cross-sectional RA epidemiological study in Greece (06/2015–05/2016, ERE RA Study Group). Demographics, disease characteristics, treatment and co-morbidity data were collected via a web-based platform

Results: 1036 RA patients treated with bDMARDs were identified during the one year recruitment period (female: 82%, mean age: 61.5±13 years, mean disease duration: 12.5±8.9 years, mean DAS28-ESR: 3.4±3.3). Among them, 26% (n=273) were receiving bDMARDs as monotherapy and 8% (n=23) of them had never tried conventional synthetic DMARDs (csDMARDs) before; The latter group (n=23) compared to the csDMARD-exposed (92%, n=250) group, had more often co-morbidities [cardiovascular disease (22% vs. 8%, p=0.029), chronic hepatitis (13% vs. 3%, p=0.02), hypertension (57% vs. 38%, p=0.08), COPD (13% vs. 4.4%, p=0.07)] or were active smokers (41% vs. 14%, p=0.001). csDMARD discontinuation was mainly due to adverse events (AEs, 58%) followed by inadequate response (IR, 44%). Compared to the cs- and b-DMARD combination therapy group, monotherapy treated patients were more frequently seropositive (64% vs. 57%, p=0.003), had lower DAS28-ESR (3.2 vs 3.5, p=0.009) and were more likely to have discontinued csDMARDs for AEs (58% vs. 21%, p<0.001) or IR (44% vs. 27%, p<0.001). Tocilizumab (22.3% vs. 12.7%, p<0.001) and rituximab (19.8% vs. 13.5%, p=0.013) were utilized more often, whereas adalimumab less often (8.8% vs. 14.8%, p=0.012) as monotherapy compared to as part of combination therapy.

Conclusions: In our large RA cohort, one out of four bDMARD treated patients, were receiving bDMARDs as monotherapy. Co-morbidities rather than RA characteristics influence the initial decision for bDMARD monotherapy whereas among those starting combination cs- and b-DMARD therapy, the majority discontinue csDMARDs due to AEs.

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SAT0177 SAFETY EVENTS ARE SIMILAR WITH ABATACEPT VS PLACEBO TREATMENT IN RA: RESULTS FROM INTEGRATED DATA ANALYSIS FROM NINE CLINICAL TRIALS

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Background: Abatacept is a selective co-stimulation modulator that consists of the extracellular domain of human cytotoxic T lymphocyte-associated antigen-4 linked to the modified Fc portion of human immunoglobulin and was approved initially for the treatment of RA in 2005. The integrated safety database for abatacept in adult RA comprises data from short- and long-term periods of 16 open-label and double-blind RA clinical trials, and combines studies of both IV and SC abatacept involving 7044 total patients. Of these, data from the 9 double-blind, placebo-controlled studies involving 4138 total patients were included in this analysis. The most recent overall safety analysis was performed in 2012 and reported IV and SC results separately.

Objectives: To provide an update of the overall abatacept safety profile based on data analysis from both IV and SC trials.

Methods: This evaluation included all patients with RA enrolled in 9 key double-blind, placebo-controlled clinical trials of IV and/or SC abatacept. The safety analysis includes all serious adverse events (SAEs), as well as AEs of interest including infections, malignancies and autoimmune diseases.

Results: In total, 2653 patients were exposed to abatacept and 1485 received placebo. During the double-blind, controlled period, the mean (SD) duration of exposure was 10.3 (3.5) months for the placebo group and 10.8 (3.3) months for the abatacept group for a total exposure of 2357 and 1254 patient years, respectively (Table 1). The proportion of patients as well as incidence rates for death, SAEs, infections, malignancy and autoimmune diseases were similar between those treated with abatacept and placebo (Table 2).

Conclusions: In a large RA clinical trial database, safety events including deaths, serious infections, opportunistic infections, malignancies and autoimmune diseases occurred at similar frequencies and rates in the abatacept and placebo treatment groups.

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Table 1. Demographic Data

	Abatacept (N=2653)	Placebo (N=1485)
Mean age, yr (SD)	51.7 (12.4)	51.4 (12.3)
Female, %	79.1	79.7
White, %	86.1	86.5
NSAIDs, %	79.0	79.6
Glucocorticoids, %	51.6	49.4
Mean oral dose, mg (SD)	7.5 (8.1)	9.1 (9.1)
MTX, %	68.2	63.8
Anti-TNF, %	6.4	5.5

Table 2. Events During the Double-Blind, Placebo-Controlled Period

Outcome	Abatacept (N=2653)		Placebo (N=1485)	
	N (%)	IR (95% CI)	N (%)	IR (95% CI)
Deaths	12 (0.5)	0.5 (0.3, 0.9)	12 (0.8)	1.0 (0.5, 1.7)
SAEs	331 (12.5)	14.8 (13.3, 16.5)	174 (11.7)	14.6 (12.5, 17.0)
Discontinued due to SAEs	68 (2.6)		22 (1.5)	
Infections	1440 (54.3)	91.3 (86.7, 96.2)	761 (51.6)	90.8 (84.4, 97.4)
Serious infections	41 (1.5)	1.7 (1.2, 2.3)	16 (1.1)	1.2 (0.7, 2.0)
Solid organ malignancies	26 (1.0)	1.11 (0.7, 1.6)	12 (0.8)	1.0 (0.5, 1.7)
NMISC (combined)	14 (0.5)	0.6 (0.3, 1.0)	5 (0.3)	0.4 (0.1, 0.9)
Autoimmune diseases	198 (7.5)	8.5 (7.3, 9.8)	115 (7.7)	9.2 (7.6, 11.1)
COPD	13 (0.5)	0.6 (0.3, 1.0)	2 (0.1)	0.2 (0.0, 0.6)

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SAT0178 PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS TREATED WITH BIOLOGIC

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Background: Use of biologic therapy (BT) has been determinant in Rheumatoid Arthritis' (RA) change of management and outcomes improvement for the last decade. Classic extraarticular manifestations are now uncommon, except for the pulmonary involvement, which can occur due to different causes and can complicate our patients' treatment and prognosis.

Objectives: The aim of this study is to evaluate the presence of pulmonary complication in RA patients under BT in our hospital, and assess its severity and the modifications required.

Methods: Review of clinical records of 208 RA patients receiving BT in the last 5 years (January 2012 to December 2016). 23 cases of preexisting lung disease for other causes have been excluded and finally 26 patients have been finally included. Demographic data, characteristics of RA, types of pulmonary involvement, evolution and changes in treatment have been collected. Statistical analysis were performed using SPSS v22.

Results: 73.1% are women, mean aged 59 years (31–80); 53.8% never smokers. They suffer from long term RA (median 176.92 months, SD 199.34); only 2 patients have been recently diagnosed (less than a year). They are mainly seropositive (85% RF positive) with positive CCP antibodies in 69.2%, and with erosive disease in 70%. 25% have other extraarticular manifestations (3 rheumatoid nodules, 4 cardiac involvement).

Half of the patients were in remission or low activity (DAS 28) at the time of pulmonary disease diagnosis, and the median of CRP was 0.52 mg/dL (SD 1.72). 90% had received Methotrexate and almost half of them Leflunomide; 30% had been treated with BT (50% TNF alpha inhibitors).

Interstitial lung disease (ILD) was the most frequent pulmonary involvement (57.7%) and non-specific interstitial pneumonia (NSIP) the most prevalent pattern (>60%). We also found obstructive pulmonary disease (11.5%) and vascular involvement (7.7%). 40% of the patients had a normal radiograph (all of them a pathological CT).

Treatment was modified in 53.8% of the cases (synthetic DMARD was kept in 68% and BT in 64%).

The average time of evolution of pulmonary involvement is 37.85 months (1–156). 80% of the patients kept stable or improved from their arthritis and also from respiratory disease. Only one received a lung trasplant and another one died.

We haven't found an association between different types of pulmonary involvement and the different variables analyzed in the study. We didn't show significant differences in prognosis related to pulmonary disease distinct patterns; up to 80% of patients with ILD stabilize or improve.

Conclusions: Prevalence of pulmonary disease in our experience in RA patients under BT is similar to prevalence in other observational studies (10–20%), because diagnosis here is due to casual detection in a routine chest X-ray or for clinical suspicion for respiratory symptoms (cough, dyspnea, ...). The evolution has been good perhaps for the high prevalence of NSIP, which requires less therapeutic intervention. Protocols for systematic search of lung disease in RA patients seem essential for its proper diagnosis, and there is a need for further research in pathogenesis and management of this complication.

Disclosure of Interest: None declared
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SAT0179 THE ASP358ALA VARIANT IN THE IL6R GENE IS SIGNIFICANTLY ASSOCIATED WITH DIFFERENCES IN SOLUBLE IL-6R PROTEIN LEVELS BUT NOT WITH DIFFERENCES IN SARILUMAB RESPONSE IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: Sarilumab is a human mAb that blocks IL-6 from binding to both membrane-bound and soluble IL-6Rα (sIL-6R). A missense variant in the *IL6R* gene, Asp358Ala (rs2228145), falls within a proteolytic cleavage site and individuals with an alanine at this position have increased sIL-6R in circulation.¹ In addition, this variant has been associated with several diseases including RA.²

Objectives: To determine the impact of the Asp358Ala variant on sIL-6R concentrations and response of RA patients to sarilumab.

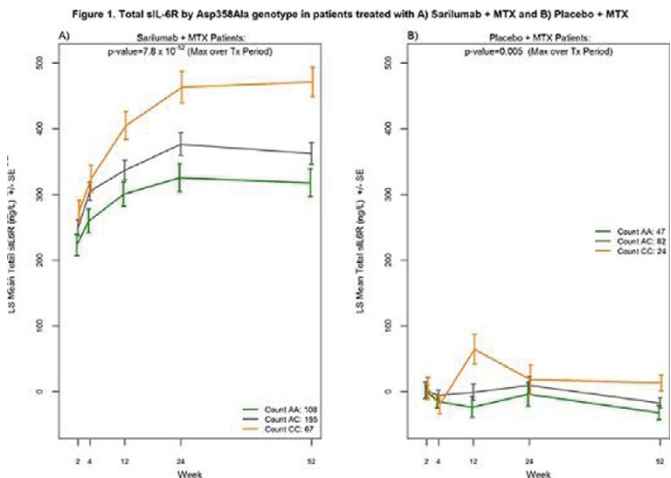
Methods: DNA was collected from patients enrolled in the MOBILITY study (NCT01061736) that evaluated the efficacy and safety of sarilumab + methotrexate (MTX) in RA patients with inadequate response to MTX. The pharmacogenetic analysis was conducted on 599 Caucasian patients (396 sarilumab 150 or 200 mg q2w + MTX, 203 placebo + MTX).

Results: Concentrations of sIL-6R were strongly associated with the Asp358Ala genotypes at baseline ($p=4.2 \times 10^{-11}$). The difference in sIL-6R concentrations between genotype groups continued to increase in sarilumab-treated patients through the end of treatment, particularly for the CC genotype (Figure; $p=7.8 \times 10^{-12}$). There was a modest association for change in sIL-6R in placebo + MTX-treated patients ($p=0.0052$). Variation in Asp358Ala was not associated with sarilumab efficacy, including mTSS at week 52 and ACR scores (Table).

Table 1. Efficacy Endpoints¹ and sIL-6R Levels by Asp358Ala Genotypes in Sarilumab-Treated Patients²

Genotype	sIL-6R	mTSS ³	ACR20	ACR50	ACR70	MCR ⁴	SJC ⁵	TJC ⁶
AA (n=129)	317.7 (21.0)	1.4 (0.5)	59	40	22	13	-10.9 (0.8)	-16.5 (1.2)
AC (n=190)	362.3 (16.4)	0.7 (0.3)	65	43	22	12	-11.1 (0.6)	-18.3 (1.0)
CC (n=77)	470.8 (22.8)	0.9 (0.5)	75	48	31	17	-11.6 (1.0)	-19.1 (1.5)
p value	7.8×10^{-12}	0.89	0.06	0.67	0.57	0.71	0.25	0.20

¹sIL-6R, mTSS, SJC, TJC show LS mean (SE). Wk 24 ACR20, ACR50, ACR70, and MCR show % achieving endpoint. ²150 or 200 mg q2w doses combined. ³van der Heijde modified total Sharp score at wk 52. ⁴Major clinical response is defined as achieving and maintaining ACR70 for ≥24 consecutive weeks during the 52-wk period. ⁵Swollen joint count. ⁶Tender joint count.



Conclusions: The Asp358Ala variant in the *IL6R* gene is significantly associated

Abstract SAT0180 – Table 1. Sarilumab Efficacy in 3 Phase 3 Studies

	MOBILITY		Pbo + csDMARDs (N=181)	TARGET		MONARCH	
	Pbo + MTX (N=398)	Sarilumab 00 mg q2w + MTX (N=399)		Sarilumab 200 mg q2w + csDMARDs (N=184)	Adalimumab 40mg q2w (N=185)	Sarilumab 200 mg q2w (N=184)	
ACR20, wk 24, %	33.4	66.4*	33.7	60.9*	58.4	71.7†	
ACR50, wk 24, %	16.6	45.6*	18.2	40.8*	29.7	45.7†	
ACR70, wk 24, %	7.3	24.8*	7.2	16.3*	11.9	23.4†	
HAQ-DI, mean change from baseline ± SD							
Wk 16/12/24	-0.3±0.6	-0.6±0.6*	-0.3±0.5	-0.5±0.6*	-0.4±0.6	-0.6±0.7†	
DAS28-CRP, mean change from baseline ± SD							
Wk 24	-1.6±1.4	-3.0±1.3*	-2.0±1.2	-3.2±1.3*	-2.1±1.2	-2.9±1.3‡	
CDAI, mean change from baseline ± SD							
Wk 24	-20.3±15.8	-27.9±13.2*	-23.9±12.9	-30.4±14.5*	-25.5±12.9	-29.7±12.7‡	

*P<0.01 vs Pbo. †P<0.01 vs adalimumab. ‡Nominal P<0.01 vs adalimumab.

with differences in sIL-6R levels at baseline and after sarilumab treatment. The differences across genotypes may be due to increases in sIL-6R production. Importantly, this variant was not associated with differences in sarilumab treatment response. These data suggest that the sarilumab doses used for this clinical study saturate both the membrane and soluble forms of IL-6R and effectively block IL-6 signaling. Sarilumab provides therapeutic benefit for RA patients irrespective of their Asp358Ala genotype status.

References:

- [1] Garbers et al. *Biochim Biophys Acta*. 2014;1842:1485–1494.
- [2] Okada et al. *Nature*. 2014;506:376–381.

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Disclosure of Interest: A. Damask Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Hamilton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Hamon Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, J. Parrino Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Penn Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Lopez Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Reid Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Overton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Baras Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Shuldiner Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paulding Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc

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SAT0180 EFFICACY AND SAFETY OF SARILUMAB 200 MG Q2W ADMINISTERED AS COMBINATION THERAPY OR MONOTHERAPY IN DIFFERENT PATIENT POPULATIONS WITH ACTIVE RA

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Background: Sarilumab, a human mAb blocking the IL-6Rα, was evaluated in 3 pivotal clinical trials.

Objectives: To assess efficacy and safety of sarilumab 200 mg q2w + csDMARDs or as monotherapy (MONARCH) in adults with active RA and inadequate response or intolerance to MTX (MOBILITY/MONARCH) or TNFi (TARGET).

Methods: MOBILITY (NCT01061736) was a 52-wk study; TARGET (NCT01709578) and MONARCH (NCT02332590) were 24-wk studies. Patients were randomized to placebo (Pbo) or SC sarilumab 150 or 200 mg q2w + MTX (MOBILITY) or csDMARDs (TARGET). MONARCH patients were randomized to SC monotherapy with adalimumab 40 mg q2w or sarilumab 200 mg q2w. Efficacy endpoints assessed in all 3 studies will be presented.

Results: Within studies, baseline demographic and disease characteristics were similar among treatment groups. Sarilumab 200 mg q2w improved ACR responses, HAQ-DI, DAS28-CRP, and CDAI (Table). Treatment response with sarilumab + csDMARDs was similar in MTX-IR and TNF-IR patients and with sarilumab monotherapy. Incidence of TEAEs and SAEs with sarilumab was more frequent vs Pbo (MOBILITY, TARGET) and similar to adalimumab (MONARCH). The most common TEAEs included infections, neutropenia, and injection site reactions and occurred more often with sarilumab vs Pbo (MOBILITY, TARGET). In MONARCH, rates of infection were similar with sarilumab and adalimumab,