a human monoclonal antibody directed against the IL-6 receptor-α (TARGET [NCT01709578]; MONARCH [NCT02332590]).

Objectives: To evaluate patient-perceived impact of sarilumab on RA using the RAID scale vs either placebo + conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or adalimumab.

Methods: TARGET assessed sarilumab 150mg and 200mg added to csDMARDs vs placebo in patients with RA intolerant of or not responding to anti-TNF therapy. MONARCH assessed sarilumab 200mg monotherapy vs adalimumab 40mg monotherapy in patients with RA either intolerant of, inadequate responders to, or considered inappropriate candidates for continued treatment with methotrexate. Treatments were administered subcutaneously every 2 weeks. RAID has 7 single-item domains, each rated by patients on an 11-point numeric rating scale from 0 (absence) to 10 (extreme). A total score from 0 to 10 (with lower scores indicative of less impact of disease) is calculated by weighting responses for each item based on patient assessment of the relative importance of the item. RAID was assessed at baseline (BL), Weeks 12 and 24. Least square mean (LSM) changes from BL in total score (Weeks 12 and 24) and domains (Week 24 only) were analysed with a mixed model for repeated measures, including treatment, region, visit, and treatment-by-visit interaction (and prior csDMARD therapy in TARGET) as fixed effects and BL as a covariate. RAID was tested outside of trial hierarchy and statistical significance is not claimed; nominal p-values are provided. Post-hoc categorical change analyses were conducted to identify "responders" in the total score (improvements ≥ minimum clinically important difference from BL to Week 24 [absolute change of 3 or relative change of 50% in total score]). Patients discontinuing therapy/requiring rescue medication prior to endpoint were classified as non-responders.

Results: Sarilumab was superior (nominal $p<0.05$) to placebo (TARGET) and adalimumab (MONARCH) at Weeks 12 and 24 for RAID total score (Table). There was a greater proportion of responders in both sarilumab dose groups vs placebo at both time points (TARGET) and in sarilumab 200mg vs adalimumab at Week 24 (MONARCH). The effect of sarilumab was consistent across all 7 individual RAID domains (nominal $p<0.05$) at Week 24, except for sleep difficulties vs placebo in TARGET. Effects of placebo were highest on pain and effects of sarilumab were lowest on emotional well-being (TARGET) and coping (MONARCH).

Table. RAID total and individual domain scores at Week 24

		TARGET study			MONARCH study	
		Placebo + csDMARD (n=181)	Sarilumab SC 150 mg q2w + csDMARD (n=181)	Sarilumab SC 200 mg q2w + csDMARD (n=184)	Adalimumab 40 mg q2w (n=185)	Sarilumab SC 200 mg q2w (n=184)
Week 24						
Total RAID score	LSM change (SE)	−1.80 (0.20)	−2.55 (0.19)	−2.80 (0.18)	−2.30 (0.17)	−3.08 (0.17)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.75 (−1.28, −0.22)**	−1.01 (−1.53, −0.48)**	–	−0.78 (−1.23, −0.32)**
	% of 'responders' (MCID = 3)	20.4	33.7**	41.8***	29.7	43.5**
	% of 'responders' (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*
Pain	LSM change (SE)	−1.63 (0.20)	−2.66 (0.19)	−2.95 (0.19)	−2.34 (0.18)	−3.22 (0.18)
	LSM difference (95% CI) vs placebo/adalimumab	–	−1.04 (−1.56, −0.52)***	−1.32 (−1.84, −0.80)***	–	−0.87 (−1.36, −0.39)**
Functional disability	LSM change (SE)	−1.46 (0.19)	−2.34 (0.19)	−2.66 (0.19)	−2.25 (0.19)	−3.12 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.88 (−1.39, −0.37)**	−1.20 (−1.71, −0.68)***	–	−0.87 (−1.38, −0.37)**
Fatigue	LSM change (SE)	−1.30 (0.20)	−2.21 (0.20)	−2.40 (0.20)	−2.33 (0.20)	−3.02 (0.20)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.91 (−1.44, −0.38)**	−1.11 (−1.64, −0.58)***	–	−0.69 (−1.22, −0.15)*
Sleep difficulties	LSM change (SE)	−1.56 (0.22)	−2.07 (0.22)	−2.53 (0.22)	−2.23 (0.21)	−2.94 (0.21)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.51 (−1.10, 0.07)	−0.97 (−1.56, −0.39)**	–	−0.70 (−1.25, −0.14)*
Physical well-being	LSM change (SE)	−1.58 (0.20)	−2.19 (0.20)	−2.36 (0.19)	−2.39 (0.19)	−3.13 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.61 (−1.13, −0.08)*	−0.78 (−1.30, −0.26)**	–	−0.74 (−1.26, −0.22)**
Emotional well-being	LSM change (SE)	−1.24 (0.20)	−1.80 (0.20)	−2.20 (0.20)	−2.07 (0.20)	−2.65 (0.20)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.56 (−1.09, −0.03)*	−0.96 (−1.49, −0.43)**	–	−0.58 (−1.12, −0.04)*
Coping	LSM change (SE)	−1.32 (0.20)	−2.07 (0.20)	−2.50 (0.20)	−1.92 (0.19)	−2.56 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.75 (−1.28, −0.22)*	−1.18 (−1.70, −0.65)***	–	−0.64 (−1.15, −0.12)*

*Nominal p≤0.05 vs placebo (TARGET)/adalimumab (MONARCH); **Nominal p≤0.01 vs placebo (TARGET)/adalimumab (MONARCH); ***Nominal p≤0.0001 vs placebo (TARGET)/adalimumab (MONARCH). CI = confidence interval; csDMARDS = conventional disease-modifying anti-rheumatic drugs; LSM = least square mean; MCID = minimum clinically important difference; q2w = every 2 weeks; RAID = Reumatoid Arthritis Impact of Disease; SC = subcutaneously; SD = standard deviation; SE = standard error of the mean

Conclusions: Assessed using RAID, sarilumab either with csDMARDs or as monotherapy reduced the impact of RA on patients' lives to a greater extent than placebo+csDMARDs or adalimumab monotherapy, with benefits shown on total RAID and all 7 individual domain scores.

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FRI0241 THE EFFECT OF ABATACEPT ON CYTOKINE PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Pathological activation of T-cells with the overproduction of pro-inflammatory cytokines is playing a major role in the pathogenesis of rheumathoid arthritis (RA). The influence of the selective co-stimulation modulator abatacept (ABA) on the dynamics of cytokine profile in patients with RA is not fully understood.

Objectives: To assess the changes in cytokine profile in patients treated with ABA.

Methods: 44 patients with RA and an inadequate response to synthetic DMARDs or biologics were enrolled in the study. Most of them were middle aged females (46,9±13,9 years) with median RA duration 2 years (1,4–3), high disease activity (DAS28=5,2±0,8), RF-positive (80%) and ACPA-positive (79,5%). 16 healthy individuals were included in the study as control. The serum levels of IL-1, IL-6, IL-17, TNF-α, VEGF, IP-10 (pg/ml) were measured by ELISA immunoassay, YKL-40 by MicroVue immunoassay at baseline and 24 weeks. Disease activity was measured by DAS28, results were assessed every 12 weeks by EULAR criteria. ABA was administered intravenously every 4 weeks.

Results: Levels of IL-6 (2.4 (1,1–6,4) vs 0.7 (0,62–1,0), p=0,0002), YKL-40 (97 (68,4–97, 9) vs. 64 (52,4–107,5), p=0,03), IP-10 (21 (12,9–49,8) vs 14 (9,2–15,2), p=0,005) were significantly higher in patients with RA compared to control. ABA significant reduced disease activity already after 12 weeks of therapy ($p<0,05$). After 24 weeks of ABA therapy good and moderate response by EULAR criteria was achieved in 86%, low disease activity by DAS28 in 52%. By the 6-th month ABA significant decreased levels of IL-6 (1,29 (0,9–2,2, p=0,0006), IP-10 (14 (7,5–28), p=0.007) as well as MMP3: before 30.1 (13–82), after 24 weeks 10 (7.4–55), p=0.0003 and RF: before 218 (9.6–187), after 24 weeks 159 (9.7–155), p=0.02. Lowering of the IL-6 (r=0,5) and IP-10 (r=0,32) levels were significantly ($p<0.05$) associated with a decrease of DAS28.

Conclusions: ABA therapy leads to a significant reduction in serum levels of IL-6, IP-10, MMP3 and RF. The serum levels of IL-6 and IP-10 correlate with decrease activity of RA.

Disclosure of Interest: None declared

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FRI0242 ASSOCIATION BETWEEN CLINICAL AND RADIOGRAPHIC RESPONSES, AND PHYSICAL FUNCTION IN A PHASE 3 STUDY OF SARILUMAB PLUS METHOTREXATE IN PATIENTS WITH ACTIVE, MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS

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Background: In MOBILITY (NCT01061736), SC sarilumab (150 or 200 mg q2w) + MTX demonstrated efficacy in adults with RA and inadequate response to MTX. The most common TEAEs were infections, neutropenia, injection site reactions, and increased transaminases.

Objectives: To examine association between clinical response and radiographic progression and functional response (HAQ-DI) in MOBILITY.

Methods: In this post hoc analysis, associations between HAQ-DI and clinical efficacy categories (CDAI, DAS28-CRP, SDAI, and Boolean-based ACR/EULAR remission) were tested at wk 16. Trend for change from baseline (BL) in HAQ-DI across response categories was assessed using the Jonckheere-Terpstra test.

Results: Regardless of definition, percentage achieving remission (CDAI ≤2.8, DAS28-CRP <2.6, SDAI ≤3.3) or no x-ray progression was higher with sarilumab vs Pbo ($P<0.05$). Overall, there was a significant trend between magnitude of clinical response at wk 16 and improvement in physical function (Table). This trend was also observed for radiographic progression (mTSS change from BL),

Table. Change From BL in HAQ-DI at Wk 16 by Categories of Clinical and Radiographic Efficacy

	Pbo + MTX N=398		Sarilumab 150 mg q2w + MTX N=400		Sarilumab 200 mg q2w + MTX N=399		All patients* N=1197	
	n (%)	mean (SD)	n (%)	mean (SD)	n (%)	mean (SD)	n (%)	mean (SD)
CDAI								
≤2.8	13 (3)	-0.7 (0.5)	25 (7)†	-0.8 (0.6)	40 (11)†	-1.1 (0.7)	78 (7)	-0.9 (0.7)
>2.8 - ≤10	47 (12)	-0.8 (0.8)	92 (23)	-0.7 (0.6)	105 (26)	-0.8 (0.6)	244 (20)	-0.7 (0.6)
>10	315 (79)	-0.2 (0.5)	242 (61)	-0.5 (0.5)	218 (55)	-0.4 (0.5)	775 (65)	-0.3 (0.5)
DAS28-CRP								
<2.6	22 (6)	-0.7 (0.6)	88 (25)†	-0.8 (0.6)	109 (31)†	-0.9 (0.7)	219 (18)	-0.8 (0.6)
≥2.6 - ≤3.2	30 (8)	-0.6 (0.9)	59 (17)	-0.6 (0.6)	66 (19)	-0.5 (0.5)	155 (14)	-0.6 (0.6)
>3.2 - <5.1	154 (41)	-0.4 (0.5)	149 (42)	-0.5 (0.5)	149 (42)	-0.4 (0.6)	450 (38)	-0.4 (0.5)
>5.1	168 (45)	-0.1 (0.5)	61 (17)	-0.3 (0.5)	30 (8)	-0.2 (0.6)	259 (24)	-0.2 (0.5)
X-ray progression (≤0 cutoff)								
No	154 (39)	-0.3 (0.5)	191 (48)†	-0.5 (0.6)	222 (56)†	-0.6 (0.6)	550 (46)	-0.5 (0.6)
Yes	244 (61)	-0.3 (0.6)	209 (52)	-0.6 (0.5)	177 (44)	-0.5 (0.6)	555 (46)	-0.4 (0.6)
X-ray progression (≤0.5 cutoff)								
No	172 (43)	-0.4 (0.5)	219 (55)†	-0.5 (0.5)	257 (64)†	-0.6 (0.6)	648 (54)	-0.5 (0.6)
Yes	226 (57)	-0.2 (0.6)	181 (45)	-0.6 (0.5)	142 (36)	-0.4 (0.6)	549 (46)	-0.4 (0.6)

*$P<0.05$ for trend test. †$P<0.05$ vs Pbo for % with remission/no progression.