low rate of adverse transfusion reactions during the 18 months analyzed. The most frequent adverse reaction was shortness of breath.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6470

FRI0238 EFFECT OF BASELINE ANTI-CYCLIC CITRULLINATED PEPTIDE 3 ANTIBODY TITRE ON LONG-TERM DRUG SURVIVAL OF SUBCUTANEOUS ABATACEPT IN RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

J.C. Sarmiento-Monroy^{1,2}, N. Molano-González², M. Rodríguez-Jiménez², R.D. Mantilla^{1,2}. ¹Rheumatology, Center of Dermatology and Rheumatology (FUNINDERMA); ²Center for Autoimmune Diseases Research (CREA), Universidad del Rosario, Bogotá, Colombia

Background: Clinical response to biologics varies widely between individuals with rheumatoid arthritis (RA). To date, there are few, and in some cases, conflicting results in the personalized approach of patients with RA treated with abatacept. Only the seropositive subphenotype (anti-cyclic citrullinated peptide, CCP) was validated in several populations, including a real-life registry (ORA) [1], and non-inferiority trial (AMPLE) [2].

Objectives: To assess whether baseline anti-CCP3 antibody status and concentration correlated with drug survival of subcutaneous (SC) abatacept among patients with RA in a real-world setting.

Methods: This was a prospective study in which well-characterized patients with RA (by 1987 ACR criteria) were included from April 2014 to December 2016. Patients were evaluated at a single rheumatology outpatient center in Bogotá, Colombia. Baseline anti-CCP3 antibody status (positive/negative) and concentration were determined using an anti-CCP3 IgG ELISA (INOVA Diagnostics). Patients with a baseline anti-CCP3 IgG concentration of ≥ 20 U were considered to be positive and were further divided into equal quartiles according to concentration [Q1–Q4 (highest concentration)]. The Cox proportional hazards regression model was used to test if there were any differences in drug survival curves according to baseline anti-CCP3 antibody status and concentration. The test was performed by the coxph function of the "survival" R package [3].

Results: A total of 129 patients were included. Baseline characteristics: female gender 86%, mean age 52 ± 13 years, median disease duration 10 (IQR 11) years, and erosions 35%. Treatment background was as follows: biologic-naïve (n=54), switched from IV to SC abatacept administration (n=24), and inadequate response to at least 1 biologic disease-modifying antirheumatic drug (n=51). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy. Rheumatoid Factor and anti-CCP3 was positive in 94%, and 89%, respectively. Median titre of anti-CCP3 was 248 U (IQR 352), and number of patients in each quartile group were Q1 (22–122)=21; Q2 (123–248)=20; Q3 (249–475)=19; Q4 (476–1544)=19. According to Cox proportional hazards regression model (Fig.1), there were significant differences between survival curves for Q1 (HR 0.1; 0.02–0.60 95% IC; p=0.011), Q2 (HR 0.2; 0.06–0.94 95% IC; p=0.041), and Q3 (HR 0.2; 0.04–0.85 95% IC; p=0.030), compared to negative group at month 32.

Figure 1. Subcutaneous abatacept survival by anti-CCP3 antibody status.

Antibody-positive patients were divided into equal quartiles (Q1–Q4), representing increasing antibody concentrations. The duration of follow-up was 32 months.

Conclusions: Baseline anti-CCP3 positivity was associated with a better response for SC abatacept in a real-world setting. Patients with lowest baseline anti-CCP3 antibody concentrations had better drug survival than patients with higher concentrations. Our results highlight the importance of identification of factors associated with response to biologics in order to optimize treatment and reduce costs.

References:

- [1] Sokolove J, et al. Ann Rheum Dis. 2016;75(4):709–14.
- [2] Gottenberg JE, et al. Ann Rheum Dis. 2012;71(11):1815–9.
- [3] Therneau, T. Grambsch P. Modeling Survival Data: Extending the Cox Model. Springer-Verlag, 2000.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6682

FRI0239 RESULTS OF A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR NANOBODY, AS MONOTHERAPY IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

T. Dörner¹, M. Weinblatt², K. Van Beneden³, E.J. Dombrecht³, K. De Beuf³, P. Schoen³, R.K. Zeldin³. ¹Rheumatology and Clinical Immunology, Charité University Hospitals, Berlin, Germany; ²Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, United States; ³Abylnx Nv, Zwijnaarde, Belgium

Background: Vobarilizumab is a Nanobody® consisting of an anti-IL6 receptor domain and an anti-human serum albumin domain in development for treatment of RA.

Objectives: To assess the efficacy and safety of several dose regimens of vobarilizumab monotherapy administered subcutaneously to patients with active RA.

Methods: Patients with active RA who were intolerant to methotrexate (MTX) or for whom continued MTX treatment was inappropriate were randomized in a 1:1:1:1 ratio to 1 of the 3 blinded dose groups of vobarilizumab or to open-label tocilizumab (TCZ), all of which were given subcutaneously. Efficacy was evaluated descriptively at Week 12 using a number of widely accepted clinical endpoints. Adverse events and routine safety parameters including laboratory assessments were recorded. TCZ administered weekly or biweekly according to local labeling was included to obtain parallel descriptive information.

Results: The study enrolled 251 patients in Europe, Latin America and the United States. Baseline demographics and disease characteristics were well balanced across groups with mean DAS28_{CRP} between 5.9 and 6.2.

Week 12 (% of patients)	Vobarilizumab 150mg q4w (N=62)	Vobarilizumab 150mg q2w (N=62)	Vobarilizumab (N=63) 225mg q2w (N=63)	Tocilizumab 162mg q1w (N=60) q2w (N=4)
ACR20	73	77	81	78
ACR50	44	37	49	45
ACR70	16	24	21	23
HAQ-DI score decrease ≥ 0.25	65	68	71	72
DAS28 _{ESR} <2.6	34	21	40	25
DAS28 _{CRP} <2.6	26	27	41	27
SDAI remission	8	5	8	11
CDAI remission	10	5	6	9

At Week 12, 73% to 81% of the patients assigned to one of the vobarilizumab groups achieved an ACR20 response, while ACR50 and ACR70 response rates between 37 - 49% and 16 - 24%, respectively, were observed (see table). At the end of the 12-week treatment period, clinically meaningful improvement in HAQ-DI scores and remission based on DAS28_{CRP} and DAS28_{ESR} was observed in a substantial number of patients treated with vobarilizumab, either q4w or biweekly. Between 5% and 10% of the patients achieved remission defined by the more stringent CDAI or SDAI criteria. In total, 94% of patients randomized to open-label TCZ received drug weekly. In spite of this disparity in dosing frequency similar efficacy results were obtained in the vobarilizumab and TCZ groups.

One vobarilizumab treated patient (225mg q2w treatment group, 1.6%) experienced a SAE during the treatment period as did 2 patients in the TCZ group (3.1%). Frequencies of treatment-emergent adverse events were similar across the groups. Of the vobarilizumab treated patients, 2.1% discontinued study drug due to TEAEs compared with 6% in the TCZ group. One case of severe hypersensitivity, not considered serious, was reported in the 225mg q2w treatment group. Liver function abnormalities were infrequent across all study groups. Grade 3 neutrophil toxicities were less commonly observed with vobarilizumab (1.1%) than with TCZ (4.3%).

Conclusions: In patients with active RA, treatment with vobarilizumab monotherapy had a positive impact on disease activity with no unexpected safety findings.

Disclosure of Interest: T. Dörner Consultant for: Abylnx, M. Weinblatt Consultant for: Abylnx, K. Van Beneden Employee of: Abylnx, E. Dombrecht Employee of: Abylnx, K. De Beuf Employee of: Abylnx, P. Schoen Employee of: Abylnx, R. Zeldin Employee of: Abylnx

DOI: 10.1136/annrheumdis-2017-eular.3746

FRI0240 RHEUMATOID ARTHRITIS (RA) IMPACT FOLLOWING TREATMENT WITH SARILUMAB: PATIENT REPORTED OUTCOMES USING THE RAID SCALE FROM TWO RANDOMIZED PHASE III TRIALS

L. Gossec¹, V. Strand², C. Proudfoot³, C. Chen⁴, S. Guilloinneau⁵, T. Kimura⁴, H. van Hoogstraten⁶, E. Mangan⁴, M. Reaney³. ¹Université Pierre et Marie Curie and Hôpital Pitié-Salpêtrière, Paris, France; ²Stanford University, Palo Alto, United States; ³Sanofi, Guildford, United Kingdom; ⁴Regeneron Pharmaceuticals, Inc, Tarrytown, United States; ⁵Sanofi, Paris, France; ⁶Sanofi, Bridgewater, United States

Background: Patients with RA experience a variety of signs and symptoms and report significant physical and psychological impairment. The RA Impact of Disease (RAID) scale is a disease-specific measure of the impact of RA on patients' lives. RAID was assessed in two Phase 3 randomized trials of sarilumab,

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 $\geq$ 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).

		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 (-1.22, -0.32)**
	% of responders (MCID = 3)	20.4	33.7*	41.8***	29.7	43.5**	
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			-1.32 (-1.56, -0.52)**		-1.36 (-1.36, -0.39)**	
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
Functional disability	LSM change (SE)	-1.48 (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)**
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
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			-1.11 (-1.44, -0.38)**	-1.03 (-1.64, -0.58)**		-0.69 (-1.22, -0.15)*
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
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			-0.97 (-1.10, 0.07)	-0.97 (-1.56, -0.39)**		-0.70 (-1.25, -0.14)*
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
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			-0.78 (-1.13, -0.08)*	-0.78 (-1.30, -0.26)**		-0.74 (-1.26, -0.22)**
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
Emotional well-being	LSM change (SE)	-1.24 (0.20)	-1.80 (0.20)	-2.20 (0.20)	-2.07 (0.20)	-2.85 (0.20)	
	LSM difference (95% CI) vs placebo/adalimumab			-0.96 (-1.09, -0.03)*	-0.96 (-1.49, -0.43)**		-0.58 (-1.12, -0.04)*
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	
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			-1.18 (-1.28, -0.22)*	-1.18 (-1.70, -0.65)**		-0.64 (-1.15, -0.12)*
	% of responders (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*	

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.

Acknowledgements: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: L. Gossec Consultant for: Abbvie, Celgene, Janssen, Lilly, Novartis, MSD, Roche, and UCB, V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celltrion, CORRONA, Crescendo, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sandoz, Sanofi, and UCB, C. Proudfoot Shareholder of: Sanofi, Employee of: Sanofi, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Guillonnet Shareholder of: Sanofi, Employee of: Sanofi, T. Kimura Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, M. Reaney Shareholder of: Sanofi, Employee of: Sanofi

DOI: 10.1136/annrheumdis-2017-eular.3448

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

M.A. Borisova, G.V. Lukina, Y. Sigidin, E.L. Luchihina, D.E. Karateev, A. Novikov, E. Alexandrova, E. Aronova, S. Glukhova, E. Nasonov. *Nasonov Research Institute of Rheumatology, MOSCOW, RUSSIA, Moscow, Russian Federation*

Background: Pathological activation of T-cells with the overproduction of pro-inflammatory cytokines is playing a major role in the pathogenesis of rheumatoid 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 $\pm$ 13.9 years) with median RA duration 2 years (1.4–3), high disease activity (DAS28=5.2 $\pm$ 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 6th 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

DOI: 10.1136/annrheumdis-2017-eular.6540

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

M.C. Genovese¹, H. van Hoogstraten², W. Kampman³, S. Jayawardena², T.W. Huizinga⁴. ¹Stanford University Medical Center, Palo Alto; ²Sanofi Genzyme, Bridgewater; ³Regeneron Pharmaceuticals, Inc., Tarrytown, United States; ⁴Leiden University Medical Centre, Leiden, Netherlands

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)
$> 2.8 - \leq 10$	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)
$\geq 2.6 - \leq 3.2$	30 (8)	-0.6 (0.9)	59 (17)	-0.6 (0.6)	66 (19)	-0.5 (0.5)	155 (14)	-0.6 (0.6)
$> 3.2 - \leq 5.1$	154 (41)	-0.4 (0.5)	149 (42)	-0.5 (0.5)	149 (42)	-0.4 (0.6)	440 (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 (50 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 (50.5 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.