Conclusions: ABA appears to be effective in ILD associated-RA, including the pattern of poor prognosis (UIP).

References:
[1] Travis WD et al. J Respir Crit Care Med 2013 188:733–748.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3492

SAT0192 SARILUMAB SUPPRESSES THROMBOSIS-RELATED GENE EXPRESSION IN CIRCULATING BLOOD CELLS IN MTX-IR AND TNF-IR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

C. Paccard[1], J. Msihid[1], A. Brisacier[1], A. Damask[2], C. Paulding[2], M. Zilberstein[3], A. Boyapati[2]. *[1]Sanofi R&D, Chilly-Mazarin, France; [2]Regeneron Pharmaceuticals, Inc, Tarrytown; [3]Sanofi R&D, Bridgewater, United States*

Background: Bone and joint damage due to chronic inflammation in the synovium of patients with RA is mediated by IL-6 and other cytokines. IL-6 mediates effects inside the joint and systemically and is blocked by sarilumab, a human mAb blocking the IL-6R?. Safety and efficacy of SC sarilumab (150 or 200 mg q2w) was evaluated in combination with MTX in patients with RA and inadequate response (IR) to MTX (MOBILITY; NCT01061736) or csDMARDs in patients with RA and IR or intolerance to ≥1 TNFi (TARGET; NCT01709578).

Objectives: To compare gene expression patterns in circulating blood cells after treatment with sarilumab vs placebo in patients from MOBILITY and TARGET.

Methods: Total RNA was isolated from whole blood collected at baseline (predose) and wk 2 posttreatment in patients from MOBILITY (placebo, n=58; sarilumab 150 mg q2w, n=60; sarilumab 200 mg q2w, n=46) and TARGET (placebo, n=19; sarilumab 150 mg q2w, n=27; sarilumab 200 mg q2w, n=16). Gene expression data were generated using microarray analyses (Agilent 8 × 60k platform). Data were processed using the limma package (R Bioconductor). Background correction and quantile normalization were performed and probes with low expression were filtered; 48,109 probes were analyzed. Effect of sarilumab vs placebo on gene expression was assessed in each study using linear mixed models. *P* values were adjusted using the Benjamini-Hochberg procedure to control false discovery rate (FDR; 5% threshold).

Results: After *P* value adjustment to control FDR at 5%, 2 genes implicated in thrombosis and atherosclerosis (thrombomodulin [THBD] and platelet endothelial cell adhesion molecule 1 [PECAM-1]) were downregulated after treatment with sarilumab 200 mg q2w vs placebo in both studies (Table). These genes decreased with a fold-change (FC) ≤0.8 in both studies ($P<0.001$). An additional gene associated with coagulation, von Willebrand factor (vWF), was significantly decreased in MTX-IR but not TNF-IR patients. Numerical decreases in gene expression between sarilumab 150 mg q2w and placebo did not reach significance.

Table 1. Select Genes Regulated by Sarilumab 200 mg q2w at Week 2

	MOBILITY Sarilumab 200 mg q2w + MTX		TARGET Sarilumab 200 mg q2w + csDMARDs	
Gene	*P* value	Fold reduction[a]	*P* value	Fold reduction[a]
THBD	6.3×10^{-7}	0.67	3.9×10^{-6}	0.58
PECAM-1	1.6×10^{-9}	0.78	2.1×10^{-4}	0.78
vWF	1.3×10^{-10}	0.58	0.55	0.91

[a]Fold reduction vs placebo.

Conclusions: In patients with active RA, sarilumab may decrease thrombosis-related gene expression in circulating immune cells. Additional analysis of the serum levels of thrombosis risk proteins is needed to test the hypothesis that sarilumab treatment decreases levels of thrombosis risk factors.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, J. Msihid Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Brisacier Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Damask Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paulding Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, M. Zilberstein Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc

DOI: 10.1136/annrheumdis-2017-eular.5183

SAT0193 RA PATIENTS WITH INFLAMMATORY ANEMIA BENEFIT FROM INCREASED HEMOGLOBIN AND DECREASED FATIGUE UNDER TOCILIZUMAB THERAPY

C. Specker[1], H. Kellner[2], P. Kästner[3], C. Volberg[4], V. Braunewell[5], I. Schwarze[6], M. Aringer[7], M. Sieburg[8], M.W. Hofmann[9], J.P. Flacke[10], H.-P. Tony[11], G. Fliedner[12]. *[1]Kliniken Essen Süd, Essen; [2]Schwerpunktpraxis für Rheumatologie und Gastroenterologie, München; [3]MVZ Ambulantes Rheumazentrum Erfurt, Erfurt; [4]Rheumazentrum Neuss, Neuss; [5]Schwerpunktpraxis Rheumatologie, Mönchengladbach; [6]Praxis für Internistische Rheumatologie, Leipzig; [7]Medizinische Klinik III, Rheumatologie, Technischen Universität Dresden, Dresden; [8]Rheumatologische Gemeinschaftspraxis, Magdeburg; [9]Rheumatologie, Chugai Pharma Europe Ltd., Frankfurt; [10]Rheumatologie, Roche Pharma AG, Grenzach-Wyhlen; [11]Rheumatologie/Immunologie der Medizinischen Klinik und Poliklinik II, Universitaetsklinikum Wuerzburg, Wuerzburg; [12]Rheumapraxis, Osnabrueck, Germany*

Background: According to WHO definition approximately 15% of all patients with rheumatoid arthritis (RA) suffer from anemia (hemoglobin <13 g/dl for men and <12 g/dl for women). Interleukin 6 (IL-6) takes an active part in the pathogenesis of this inflammatory anemia.

Objectives: The 6th interim analysis of the non-interventional ICHIBAN study (NCT01194401) evaluated the occurrence of inflammatory anemia, characterized the patient population with anemia, and observed the response during intravenous Tocilizumab therapy (TCZ i.v.). Patients were subgrouped according to their anemic/non-anemic status at baseline.

Methods: Since 2010 the ICHIBAN study collects clinical data of the routine use of TCZ i.v. in RA patients. The observation period for each patient is up to two years. At the due date of the current interim analysis (Dec 10, 2015) 2999 patients were enrolled. 902 patients have completed the maximal 104 weeks observation period (Group W104).

Results: At baseline, the proportion of patients with anemia (acc. to WHO definition) was 21.4% (men) and 22.0% (women) in the group W104.

On comparison, RA patients with anemia showed, amongst others, increased inflammation parameters, a higher disease activity and higher rates of comorbidities. Already after 4 weeks with TCZ i.v. the proportion of patients with anemia improved to 12.1% (men) and 12.7% (women). After 104 weeks therapy the proportion of patients with anemia reduced further to 7.4% (men) and 8.4% (women). The relevant response parameters and laboratory values are shown in Table 1.

Despite the higher disease activity at baseline for anemic patients, the benefit was comparable for patients with and without anemia. DAS28-ESR values decreased on average by 2.9 (women) and 3.1 (men) in RA patients with anemia and by 2.7 (women) and 2.8 (men) in RA patients without, resulting in similar disease scores at the end of the observational period.

The effectiveness of TCZ i.v. was also confirmed by patient reported outcomes (PROs) via visual analogue scales (VAS). In particular, a reduction of the intensity of pain (>50%) and a reduction of fatigue (>38%) was observed (Table 1).

Table 1 Treatment response to TCZ in anemic patients (at baseline)

		Week 0 (Baseline)	Last visit with TCZ
% Anemia	male	21.4% (46/215)	7.4% (16/215)
	female	22.0% (151/687)	8.4% (58/687)
Hemoglobin [g/dl]	male	12.2 (11.8, 12.7)	13.8 (13.2, 14.7)
Median (Q1, Q3)	female	11.1 (10.3, 11.6)	12.7 (11.9, 13.4)
Erythrocytes [10^{12}/l]	male	4.5 (4.0, 4.7)	4.7 (4.3, 5.0)
Median (Q1, Q3)	female	4.1 (3.8, 4.4)	4.2 (4.0, 4.5)
CRP [mg/l]	male	42.1 (27.3, 71.2)	7.3 (1.5, 25.4)
Median (Q1, Q3)	female	30.0 (11.1, 61.0)	3.1 (1.0, 11.9)
ESR [mm/h]	male	46.5 (30.0, 68.0)	4.5 (2.0, 13.0)
Median (Q1, Q3)	female	42.0 (28.0, 74.0)	8.0 (4.0, 16.0)
DAS28-ESR			
Change from baseline	male		-3.1 ± 2.1
Mean ± SD	female		-2.9 ± 1.5
% Remission (< 2.6)	male	0.0% (0/46)	52.2% (24/46)
	female	0.0% (0/151)	45.0% (68/151)
Visual analogue scales			
Fatigue	male	62.0 (40.0, 79.0)	30.0 (10.0, 52.0)
Median (Q1, Q3)	female	65.0 (35.0, 85.0)	40.0 (15.0, 63.0)
Intensity of pain	male	70.0 (45.0, 83.0)	32.0 (10.0, 61.0)
Median (Q1, Q3)	female	65.0 (43.0, 86.0)	30.0 (12.0, 56.0)
Sleep disturbances	male	48.0 (19.0, 67.0)	12.0 (5.0, 50.0)
Median (Q1, Q3)	female	52.0 (21.0, 80.0)	38.0 (12.0, 66.0)

(CRP = C-Reactive Protein; ESR = Erythrocyte Sedimentation Rate; Q1, Q3 = 1st / 3rd quartile; SD = standard deviation)

Conclusions: At start of therapy, approximately one out of five patients documented in ICHIBAN showed anemia according to the WHO definition. During TCZ i.v. therapy a noticeable decrease in the rate of anemia and improved hemoglobin values were observed. These effects can already be seen after four weeks of treatment and continue up to the end of this study (i.e. 2 years). Despite the higher burden of disease at baseline in RA patients with anemia, TCZ i.v. therapy resulted in good clinical response rates and PROs.

Acknowledgements: We would like to thank all patients, their families, the investigators and the nurses who participated in this trial. This research was funded by Roche Pharma AG, Germany, and Chugai Pharma Europe Ltd., Germany. Support for third-party writing assistance for this abstract presentation

was provided by Roche and Chugai and performed by Ecron Acunova GmbH, Germany.

Disclosure of Interest: C. Specker Grant/research support from: Chugai, DRFZ, Consultant for: Abbvie, Janssen, Chugai, MSD, Novartis, UCB, Lilly, Boehringer, Speakers bureau: Abbvie, Celgene, Chugai, Euroimmun, MSD, Pfizer, UCB, H. Kellner: None declared, P. Kästner: None declared, C. Volberg: None declared, V. Braunewell: None declared, I. Schwarze: None declared, M. Aringer: None declared, M. Sieburg: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., Zweigniederlassung Deutschland, J. Flacke Employee of: Roche Pharma AG, Germany, H.-P. Tony Consultant for: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Pfizer, Sanofi, Lilly, MSD, Astra-Zeneca, G. Fliedner: None declared

DOI: 10.1136/annrheumdis-2017-eular.5876

SAT0194 SIRUKUMAB INTEGRATED SAFETY IN RHEUMATOID ARTHRITIS PATIENTS: ANALYSIS OF THE SIRROUND PHASE 3 DATA

D. Aletaha[1], C. Thorne[2], M. Schiff[3], M. Harigai[4], R. Rao[5], N. Goldstein[6], B. Cheng[6], C. Cohen[7], B. Hsu[6], K. Brown[7]. *[1]Medical University of Vienna, Vienna, Austria; [2]University of Toronto and Southlake Regional Health Centre, Newmarket, ON, Canada; [3]University of Colorado School of Medicine, Denver, CO, United States; [4]Tokyo Women's Medical University, Tokyo, Japan; [5]GSK Medicines Research Centre, Hertfordshire, United Kingdom; [6]Janssen Research & Development, LLC, Spring House, PA; [7]GlaxoSmithKline, Collegeville, PA, United States*

Background: Sirukumab (SIR), a human monoclonal antibody that selectively binds the IL-6 cytokine, is in development for the treatment of rheumatoid arthritis (RA). Efficacy of SIR was shown in several phase 3 trials in RA patients (pts; SIRROUND program).

Objectives: To analyze safety data from completed/ongoing studies in the SIRROUND program.

Methods: Safety comparisons included SIR 50mg q4w and 100mg q2w doses vs placebo (pbo) in the pbo-controlled period (Wk 0–18) of 2 phase 3 studies. A long-term comparison of the safety of SIR 50mg q4w and 100mg q2w for the entire program was also performed.

Results: In phase 3 studies, 2926 pts received SIR for up to 3.4y (median duration, 1.46y). During Wk 0–18, there were more adverse events (AEs), AEs leading to discontinuation, and serious AEs (SAEs) with SIR vs pbo, with cumulative rates of SAEs remaining constant over time (Table). In general, no dose effect with SIR was observed in the 18-wk or long-term analysis. Mortality rates were similar across treatment groups through 18 wks and remained stable in long-term analysis. Serious infections were more frequent in SIR-treated pts vs pbo during Wk 0–18, with similar rates through long-term analysis. Rates of gastrointestinal (GI) perforations and malignancies were low and similar across groups during the 18-wk and long-term analysis; major adverse cardiovascular event (MACE) rates were similar through 18 wks and numerically higher with SIR 50mg q4w vs 100mg q2w in long-term analysis.

Conclusions: SIR is well tolerated in pts with moderately to severely active RA. Overall, no dose relationship was observed between SIR 50mg q4w and 100mg q2w for types or frequencies of AEs.

Disclosure of Interest: D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, C. Thorne Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, M. Schiff Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson, UCB, Speakers bureau: AbbVie, M. Harigai Grant/research support from: AbbVie Japan, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Mitsubishi Tanabe Pharma, Ono Pharmaceuticals, Santen Pharmaceutical, Takeda Pharmaceutical, UCB Japan, Teijin Pharma, Consultant for: AbbVie Japan, Janssen Pharma, Chugai Pharmaceutical, Teijin Pharma, Eli Lilly Japan, and Zenyaku Kogyo, R. Rao Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, N. Goldstein Employee of: Janssen Research & Development, LLC, B. Cheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, C. Cohen Employee of: GlaxoSmithKline, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Brown Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline

DOI: 10.1136/annrheumdis-2017-eular.5176

SAT0195 RITUXIMAB SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

D. Choquette[1], L. Bessette[2], B. Haraoui[1], F. Massicotte[1], J.-P. Pelletier[1], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], É. Villeneuve[1], L. Coupal[1]. *[1]Rheumatology, Institut de recherche en rhumatologie de Montréal (IRRM), Montréal; [2]Rheumatology, Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, Canada*

Background: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option,

Abstract SAT0194 – Table 1. Treatment-emergent AEs in Phase 3 Studies

	Wk 0–18			Long-term analysis (Wk 0-safety cutoff)	
Ine	Pbo (N=850)	SIR 50mg q4w (N=848)	SIR 100mg q2w (N=850)	SIR 50mg q4w (N=1461)	SIR 100mg q2w (N=1465)
AEs, n (%)	444 (52.2)	515 (60.7)	548 (64.5)	1207 (82.6)	1237 (84.4)
AEs leading to discontinuation, n (%)	22 (2.6)	34 (4.0)	45 (5.3)	174 (11.9)	196 (13.4)
SAEs, n (%)	27 (3.2)	41 (4.8)	46 (5.4)	265 (18.1)	268 (18.3)
Incidence*	9.36 (6.17–13.61)	14.36 (10.30–19.48)	16.14 (11.82–21.53)	13.12 (11.58–14.79)	13.12 (11.60–14.79)
Serious infection, n (%)	7 (0.8)	16 (1.9)	14 (1.6)	102 (7.0)	101 (6.9)
Incidence*	2.40 (0.97–4.95)	5.52 (3.15–8.96)	4.81 (2.63–8.07)	4.76 (3.88–5.77)	4.67 (3.81–5.68)
GI perforation, n (%)	0	1 (0.1)	3 (0.4)	5 (0.3)	9 (0.6)
Incidence*	0 (0–1.02)	0.34 (0.01–1.91)	1.02 (0.21–2.99)	0.23 (0.07–0.53)	0.41 (0.19–0.77)
MACE, n (%)	2 (0.2)	3 (0.4)	2 (0.2)	20 (1.4)	9 (0.6)
Incidence*	0.68 (0.08–2.47)	1.03 (0.21–3.00)	0.68 (0.08–2.46)	0.92 (0.56–1.42)	0.41 (0.19–0.77)
Malignancy, n (%)	2 (0.2)	1 (0.1)	1 (0.1)	23 (1.6)	19 (1.3)
Incidence*	0.68 (0.08–2.47)	0.34 (0.01–1.91)	0.34 (0.01–1.91)	1.05 (0.67–1.58)	0.86 (0.52–1.35)
Death, n (%)	1 (0.1)	1 (0.1)	1 (0.1)	15 (1.0)	14 (1.0)
Incidence*	0.34 (0.01–1.91)	0.34 (0.01–1.91)	0.34 (0.01–1.90)	0.68 (0.38–1.13)	r 0.63 (0.35–1.06)

*Incidence per 100 pt-years (95% CI).

Abstract SAT0195 – Table 1. First bDMARD history and Retention Characteristics of Second bDMARD used

	Second bDMARD					
	TNFi			Rituximab		
First bDMARD Failed	Failure type		All	Failure type		All
	Primary	Secondary		Primary	Secondary	
TNF inhibitor	41 (25.5%)	120 (74.5%)	161 (100.0%)	17 (28.8%)	42 (71.2%)	59 (100.0%)
Other mode of action	6 (18.2%)	27 (81.8%)	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	47 (24.2%)	147 (75.8%)	194 (100.0%)	17 (28.8%)	42 (71.2%)	59 (100.0%)
Second bDMARD Retention Probability at:						
6 Months		64.68% (3.45%)			96.15% (2.67%)	
12 Months		50.54% (3.61%)			88.05% (4.59%)	
24 Months		39.77% (3.59%)			85.84% (4.97%)	
60 Months		22.26% (3.53%)			72.44% (6.95%)	
96 Months		13.22% (3.62%)			72.44% (6.95%)	
Biologic Retention Time (years)						
Mean, mean (SE)		2.71 (0.25)			6.73 (0.46)	
Lower Quartile, (95% CI)		0.36 (0.28–0.44)			4.18 (1.51–8.48)	
Median, (95% CI)		1.08 (0.71–1.60)			– (8.42 –)	
Upper Quartile, (95% CI)		4.26 (3.25–6.64)			– (–)	