was 64% lower among pts treated with ABA vs placebo. After adjusting for heterogeneity across studies, the frequency (95% CI) of OI remained lower for the ABA group (0.15% [0.06, 0.42] vs the placebo group (0.48% [0.22, 1.04]).

Conclusions: Abatacept-treated pts had a lower incidence rate of OI compared with placebo. The OI and herpes infection incidence rates in the cumulative data are similar or lower to those reported in the literature.[1–3]

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OP0102 PATIENT REPORTED BENEFITS OF SARILUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN ADULT PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

V. Strand[1], L. Gossec[2], C. Proudfoot[3], C. Chen[4], M. Reaney[3], S. Guillonneau[5], T. Kimura[4], J. van Adelsberg[4], Y. Lin[6], E. Mangan[4], H. van Hoogstraten[6], G.R. Burmester[7]. *[1]Stanford University, Palo Alto, United States; [2]Universite Pierre et Marie Curie and Hopital Pitie-Salpetriere, Paris, France; [3]Sanofi, Guildford, United Kingdom; [4]Regeneron Pharmaceuticals, Inc., Tarrytown, United States; [5]Sanofi, Paris, France; [6]Sanofi, Bridgewater, United States; [7]Charité - University Medicine, Berlin, Germany*

Background: The phase 3 MONARCH superiority study (NCT02332590) compared efficacy and safety of sarilumab (a human anti-IL-6Rα monoclonal antibody [mAb]) 200 mg administered subcutaneously every 2 weeks (q2w), with adalimumab (an anti-TNF-α mAb) 40 mg administered q2w, in patients with active rheumatoid arthritis (RA) who were either intolerant of, or inadequate responders to methotrexate treatment. Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in reduction of disease activity and improvements in physical function and signs and symptoms of RA, with safety and tolerability consistent with IL-6R or TNF blockade.

Objectives: To compare patient-reported outcomes (PROs) with sarilumab vs adalimumab from MONARCH.

Methods: PROs assessed at baseline, weeks 12 and 24 included ACR components (Patient Global Assessment of Disease Activity [PtGA], Pain visual analog scale [VAS], Health Assessment Questionnaire Disability Index [HAQ-DI]), Medical Outcomes Study Short Form-36 (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Morning Stiffness VAS, RA Impact of Disease (RAID) and RA-specific Work Productivity Survey (WPS-RA). Least-squares mean (LSM) between-group differences were determined by mixed-model for repeated measures with treatment, visit, treatment-by-visit interaction and region as fixed effects, and the corresponding baseline PRO scores as continuous covariates. A *P*-value <0.05 was considered statistically significant for PROs in a predefined hierarchy (ACR components, SF-36 physical component summary [PCS], FACIT-F and SF-36 mental component summary [MCS] scores). For PROs not in the hierarchy, significance is not claimed. Changes from baseline were compared with published values for minimum clinically important differences (MCIDs).

Results: Baseline demographics, disease characteristics and PROs were generally balanced between treatment groups (n=184 sarilumab; n=185 adalimumab). Improvements from baseline to week 24 were greater with sarilumab vs adalimumab across PtGA, Pain VAS, HAQ-DI, SF-36 PCS, Morning Stiffness VAS, RAID and WPS-RA global scores (all $P<0.05$, statistical significance is claimed only for PROs in the hierarchy; see table). Between-group differences in FACIT-F and SF-36 MCS scores were not significant. Improvements ≥MCID were reported by a greater percentage of patients with sarilumab than adalimumab for HAQ-DI (≥0.22 units), RAID (≥3 units), SF-36 PCS (≥2.5), and Morning Stiffness VAS (≥10) (all nominal $P<0.05$).

Table. Mean change from baseline to week 24 with sarilumab 200 mg q2w or adalimumab 40 mg q2w

PRO	Mean (SD) Baseline score		LSM Changes (SE) from Baseline to Week 24		Least-Squares Mean Between-Group Difference (95% CI)	*P*-value*
	Sarilumab 200 mg q2w (n=184)	Adalimumab 40 mg q2w (n=185)	Sarilumab 200 mg q2w (n=184)	Adalimumab 40 mg q2w (n=185)		
ACR components						
HAQ-DI	1.64 (0.54)	1.62 (0.64)	-0.61 (0.05)	-0.43 (0.05)	-0.18 (-0.31, -0.06)	<0.005
Pain VAS	70.93 (18.77)	70.32 (19.31)	-36.19 (1.78)	-27.41 (1.80)	-8.78 (-13.66, -3.90)	<0.001
PtGA	68.22 (17.38)	67.51 (18.27)	-33.30 (1.73)	-24.82 (1.75)	-8.48 (-13.24, -3.72)	<0.001
SF-36						
PCS	30.77 (6.09)	31.53 (6.48)	8.74 (0.56)	6.09 (0.56)	2.65 (1.15, 4.15)	<0.001
MCS	36.43 (10.43)	36.93 (11.59)	7.86 (0.77)	6.83 (0.77)	1.04 (-1.06, 3.13)	0.332
Physical functioning	33.26 (19.68)	35.53 (22.01)	22.38 (1.64)	15.01 (1.65)	7.37 (2.91, 11.83)	<0.005
Role-physical	34.31 (18.03)	34.89 (20.51)	20.80 (1.61)	16.23 (1.63)	4.57 (0.18, 8.96)	<0.05
Bodily pain	36.77 (15.84)	39.15 (16.87)	25.69 (1.46)	19.40 (1.47)	6.28 (2.32, 10.25)	<0.005
General health	34.00 (16.03)	36.45 (15.85)	13.96 (1.18)	11.05 (1.19)	2.91 (-0.30, 6.12)	0.076
Vitality	33.29 (16.35)	35.51 (17.39)	17.95 (1.42)	14.39 (1.43)	3.56 (-0.31, 7.43)	0.071
Social functioning	46.27 (23.18)	47.55 (26.18)	21.41 (1.81)	15.04 (1.83)	6.37 (1.43, 11.30)	<0.05
Role emotional	47.15 (24.38)	47.57 (27.15)	18.04 (1.79)	14.10 (1.81)	3.94 (-0.94, 8.82)	0.113
Mental health	48.16 (18.01)	49.81 (19.44)	14.29 (1.31)	13.26 (1.32)	1.02 (-2.54, 4.58)	0.572
FACIT-F	23.59 (8.92)	24.43 (10.26)	10.18 (0.70)	8.41 (0.71)	1.77 (-0.14, 3.67)	0.069
Morning stiffness VAS	70.76 (18.93)	68.95 (21.42)	-36.08 (1.95)	-29.29 (1.97)	-6.80 (-11.10, -0.50)	<0.05
RAID	6.89 (1.69)	6.28 (2.06)	-3.08 (0.17)	-2.30 (0.17)	-0.78 (-1.23, -0.32)	<0.001
WPS-RA (global)†	N/A	N/A	N/A	N/A	N/A	<0.005

*Least-squares mean between-group differences (sarilumab vs adalimumab).
Items above the dotted line were part of the hierarchy and thus statistical significance may be claimed. Between-group differences were not significant for FACIT-F and SF-36 MCS. Items below the dotted line are outside of the hierarchy and thus statistical significance is not claimed and nominal *P*-values are provided.
†Global test for the chance from baseline in the eight WPS-RA scores.

Conclusions: Sarilumab monotherapy compared with adalimumab monotherapy resulted in greater and clinically meaningful improvements in many PROs, including patient-reported disease activity, pain, physical function, morning stiffness, productivity, health related quality of life and health status.

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OP0103 THE EFFECT OF SIRUKUMAB PLUS METHOTREXATE ON CIRCULATING BIOMARKERS OF JOINT DESTRUCTION IN MODERATE TO SEVERE RHEUMATOID ARTHRITIS PATIENTS FROM THE SIRROUND-D PHASE 3 STUDY

B. Dasgupta[1], K. Campbell[1], A.-C. Bay-Jensen[2], M. Karsdal[2], K. Sweet[1], M. Sims[3], M.J. Loza[1]. *[1]Janssen Research & Development, LLC, Spring House, PA, United States; [2]Nordic Bioscience, Herlev, Denmark; [3]GlaxoSmithKline, Stevenage, United Kingdom*

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation that can lead to progressive bone and joint damage. The cytokine interleukin-6 (IL-6) is implicated in inflammatory pathways associated with bone and cartilage degradation in RA. Inhibition of IL-6 signaling by sirukumab (SIR), an anti-IL6 cytokine monoclonal antibody, was shown to significantly reduce structural damage progression, relative to placebo (pbo), in disease-modifying antirheumatic drug inadequate responder (DMARD-IR) RA patients (pts) in the Phase 3 SIRROUND-D study.

Objectives: To investigate the mechanism of SIR on joint tissue remodeling, a panel of serum biomarkers associated with matrix metalloproteinase (MMP)-driven interstitial matrix and basement membrane degradation (C1M, C3M, C4M), bone turnover (β-isomerized C-terminal telopeptides of type I collagen, CTX-I), osteoblast formation (osteocalcin/NMID), synovial destruction (MMP-3), and tissue inflammation (MMP-mediated destruction of CRP/CRPM) were assessed in pts with moderate to severe RA from SIRROUND-D.

Methods: Serum samples from a sub-cohort of SIRROUND-D (for whom radiographic data were available) were analyzed ad hoc for the following biomarkers: C1M, C3M, C4M, CRPM, MMP-3, CTX, and osteocalcin. Samples from 100 pts treated with pbo and methotrexate (MTX) and 100 pts treated with SIR 50mg q4w + MTX were tested. Biomarkers were measured in all pts at baseline (BL) and Wk 4; samples from SIR and pbo-treated pts (50/group) were tested at Wk 52. Differences between groups were evaluated by comparing within-subject $\log_2$ ratio of Wk 4 or Wk 52 over BL values between treatment groups. Structural damage progressors versus non-progressors were defined based on changes from BL in Sharp/van der Heijde score (SHS) at Wk 52 (≥5 vs <5). Differences between groups were tested using General Linear Models.

Results: SIR significantly reduced serum levels of C1M (-48%), C3M (-30%), C4M2 (-42%), and CRPM (-22%) by Wk 4 vs pbo ($P<0.001$), with similar reductions observed at Wk 52; MMP-3 levels were more substantially decreased by SIR at Wk 52 (-39%) vs Wk 4 (-20%). In contrast, treatment with SIR resulted in increased levels of CTX-I (+20%) and osteocalcin (+12%) by Wk 4 ($P<0.001$; Figure 1). As 95% of the total study population included in this biomarker analysis did not progress (defined as ≥5 Wk 52 change in SHS), we were unable to demonstrate an association between changes in pharmacodynamic markers and radiographic progression. Nor were significant associations with pharmacodynamic changes with SIR treatment observed for comparisons among patients grouped by Wk 52 changes in SHS of ≥5 (n=5), <5 to ≥0.5 (n=41),

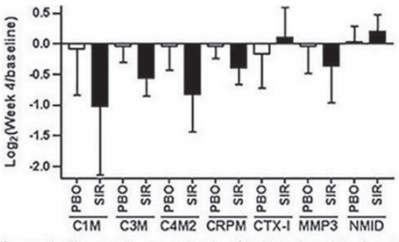

Figure 1. Changes in serum levels of indicated analyte (x-axis), displayed as mean ± SD of log2-transform of within-subject week 4/baseline ratios, stratified by treatment group (PBO, placebo; SIR, sirukumab 50mg q4w). P<0.05 for SIR vs. PBO for each analyte.