regardless of cutoff (≤0.5 and ≤0). In patients achieving remission, there was a numerically greater improvement in HAQ-DI with sarilumab vs placebo (Pbo). Even if patients did not achieve remission or LDA, the sarilumab group had generally greater numerical improvements in HAQ-DI vs Pbo.

Conclusions: Achieving LDA or remission, or absence of radiographic progression, was associated with overall greater improvement in physical function. Irrespective of whether patients achieved remission or LDA, sarilumab + MTX showed greater improvements in HAQ-DI than Pbo + MTX.

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FRI0243 SIRUKUMAB TREATMENT REDUCES LEVELS OF IRON-REGULATORY PROTEINS AND AMELIORATES INFLAMMATION-ASSOCIATED ANEMIA IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Anemia of chronic disease, a common comorbidity of rheumatoid arthritis (RA), is detrimental to patients' (pts) quality of life, productivity, and long-term health.

Objectives: Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, has recently demonstrated efficacy in RA. It was hypothesized that SIR, compared to placebo (pbo) and tumor necrosis factor-inhibitors (TNFi), increases hemoglobin (Hb) concentrations in RA pts by decreasing levels of iron-scavenging proteins and increasing transferrin levels, thus ameliorating anemia. This hypothesis was tested in post hoc analyses of 4 phase 3 studies of SIR in RA: SIRROUND-M (methotrexate [MTX] inadequate responders [IR]); -D (disease-modifying antirheumatic drug [DMARD] IR); -T (TNFi-IR); -H (MTX-IR, monotherapy).

Methods: Standard hematology measurements, including Hb levels, were made throughout the studies by a central laboratory. Anemia was defined as Hb levels <125 g/L (males) and <115 g/L (females). In a subset of pts, iron-regulatory proteins (hepcidin, haptoglobin, hemopexin, transferrin) were measured in serum at baseline (BL) and Wk 4 using the SomaLogic SOMAscan™ platform (for SIRROUND-M, -D, -T, and -H studies, respectively: SIR 100mg q2w, n=61, 205, 136, 0; SIR 50mg q4w, n=61, 201, 128, 100; pbo, n=0, 118, 56, 0; adalimumab [ADA], n=0, 0, 0, 98).

Results: SIR consistently reduced the prevalence of anemia to a greater extent than was observed for pbo ($p<0.05$; eg, in SIRROUND-D, anemia decreased from 25% of pts at BL to 10% at Wk 16 post-treatment with SIR 50mg q4w vs increase from 24% of pts to 28% with pbo) and ADA (SIRROUND-H). Across studies on SIR 50mg q4w, increases in Hb levels ranged from 7±10 to 10±11 g/L (mean±SD) through Wk 16; however, greater changes were seen in pts anemic at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed by Wk 2, with comparable results for SIR 100mg q2w. Statistically significant increases in Hb levels were not observed with ADA (Fig.1) or pbo, regardless of BL anemia status. Changes in Hb levels with SIR were independent of changes in RA disease activity. Mean haptoglobin levels were modestly higher at BL in RA pts with anemia compared to pts without anemia. Across studies, both SIR doses similarly strongly decreased levels of hepcidin, haptoglobin, and hemopexin and increased transferrin levels at Wk 4, regardless of BL anemia status. The modulation of these proteins by ADA was considerably less (Fig.1) and by pbo non-significant. After SIR treatment, greater decreases in hepcidin levels were consistently observed in pts with vs without BL anemia across studies by Wk 4.

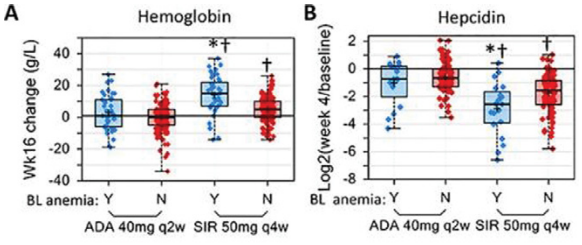

Figure 1. For the SIRROUND-H study, changes in (A) hemoglobin (week 16 change from baseline in g/L) and (B) hepcidin (log_2(week 4/baseline)) are plotted for each available patient, stratified by treatment group and baseline (BL) anemia status (Y, blue; N, red). * p<0.05 for baseline anemia Y vs. N within treatment group; † p<0.05 vs. adalimumab, within baseline anemia group. ADA, adalimumab; SIR, sirukumab.

Conclusions: SIR consistently increased Hb levels in RA pts (DMARD-IR, TNFi-IR, monotherapy), most prominently in pts with BL anemia, resulting in significant reductions in the prevalence of anemia. These effects were independent of the extent of improvement in RA disease activity, suggesting additional benefits of SIR beyond clinical response in RA. By inhibiting IL-6, SIR may decrease key iron-regulatory proteins, such as hepcidin, and shift homeostasis towards an increase in the pool of iron available for red blood cell Hb, thus ameliorating anemia of chronic inflammation associated with RA.

Disclosure of Interest: M. Loza Employee of: Janssen Research & Development, LLC, K. Campbell Employee of: Janssen Research & Development, LLC, K. Sweet Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, S. Daga Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, B. Dasgupta Employee of: Janssen Research & Development, LLC

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FRI0244 LOW DOSE OF RITUXIMAB IS EFFECTIVE FOR MAINTENANCE OF CLINICAL REMISSION OR LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Although existing data support the effectiveness of the low dose regimen (LDR, 1gr every 6 months) of rituximab as initial treatment for active rheumatoid arthritis (RA) (2), it is unknown whether this regimen may be used to maintain the therapeutic effect in patients achieved clinical remission or low disease activity (LDA) upon treatment with conventional rituximab regimen (2gr every 6 months)

Objectives: To evaluate the effectiveness of the rituximab LDR for maintenance of clinical remission and/or LDA in patients with RA in clinical practice.

Methods: Long-term prospective study of RA patients who received rituximab in the Rheumatology Department of the University Hospital of Heraklion during 03/2005–07/2016. All patients on clinical remission [DAS 28 (ESR) <2.6] or LDA [DAS28 (ESR) <3.2] for at least 12 months were treated with the LDR after obtaining verbal consent.

Results: We analyzed 247 patients who received conventional rituximab regimen, of median age (IQR) 62 (54.3–70.4)years, females (84%), disease duration 9.6 (5.6–18.3) years,52% seropositive (RF or anti-CCP). Patients have had failed in (median) 3 (2–3) non-biologic (nbDMARDs) and 1 (1–2) biologic DMARDs (bDMARDs) before rituximab initiation. At baseline of rituximab treatment, 58.3% and 91.1% of them were on steroids and (nbDMARDs) respectively, while the disease activity was high [mean DAS28 (ESR): 5.84 (5.20–6.49)] and they had impaired physical functioning [mean HAQ: 1.0 (0.63–1.38)].

Overall, 27/247patients (11%) received the LDR. Before the initiation of LDR, the duration of rituximab treatment was 24 (18–48) months and cumulative rituximab "exposure" was 8 (6–15) gr. At the time of LDR initiation, disease activity [DAS28 (ESR)] was 2.8 (2.2–3.6) and HAQ: 0 (0–0.4), while the time needed for achieving remission or LDA was18 (8–23) months. The median duration of follow-up of patients on LDR was12 (6–20) months. 23 (85%) of patients remained in remission or LDA with median DAS28 (ESR) 2.85 (2.23–3.52) and HAQ 0 (0–0.5) at last follow-up. Only 3 (11%) of the patients experienced an increase of DAS28 (>1.2) and 2 (7%) of patients return to conventional dose.

Conclusions: In clinical practice, RA patients who achieved remission or low disease activity with conventional dose of rituximab may sustain clinical responses if treated with LDR. These preliminary findings support the use of LDR as maintenance treatment regimen and this may allow cost savings. (1)

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[2] Chatzidionysiou K, et al. Effectiveness of two different doses of Rituximab for the treatment of rheumatoid arthritis in an international cohort: data from the CERERRA collaboration. Arthritis Res Ther. 2016; 18:50.

Disclosure of Interest: None declared

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FRI0245 ABATACEPT RETENTION RATES AND PROGNOSTIC FACTORS OF RETENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: 2-YEAR RESULTS FROM THE REAL-WORLD ACTION STUDY

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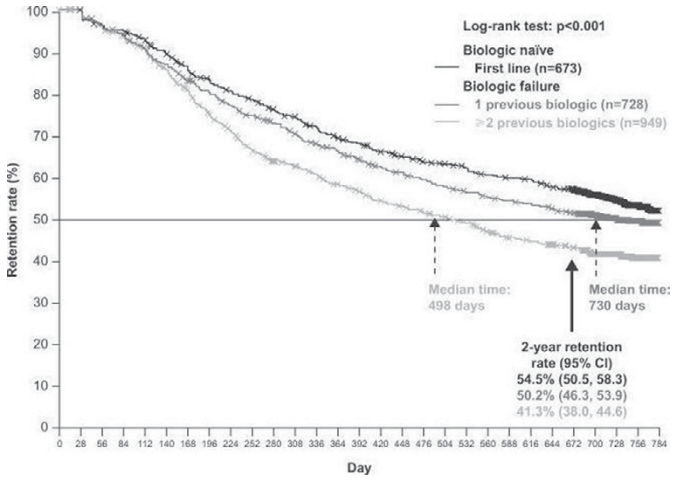
Background: The ACTION (NCT02109666) study was designed to provide

prospective, real-world data on abatacept (ABA) retention in patients (pts) with RA.

Objectives: To assess the retention rate and to identify prognostic factors of ABA retention in the overall ACTION population and by treatment line over 2 yrs.

Methods: ACTION is a 2-yr, international, observational study of pts with RA who initiated IV ABA as first- or as second-/further-line biologic therapy in routine clinical practice. Biologic-naïve and biologic-failure pts were enrolled during three periods between May 2008 and December 2013. The primary endpoint was crude ABA retention rate over 2 yrs (Kaplan–Meier plot). Prognostic factors ($p \leq 0.2$) from univariate analyses with no colinearity, clinically relevant variables and known risk factors were entered into a multivariate model; factors with $p \leq 0.1$ were retained by backward selection. EULAR response was compared by Fisher's exact test.

Results: In the ACTION cohort, 2350/2364 enrolled pts were evaluable for analysis; 673 (28.6%) were biologic naïve and 1677 (71.4%) had failed biologic treatment. Most biologic-failure pts (56.6%) had previously received ≥2 biologics. Some expected differences in baseline characteristics were observed between groups; mean (SD) RA duration was shorter (7.2 [8.2] vs 12.1 [9.1] yrs; $p<0.001$), more pts had RA for ≤2 yrs (35.7 vs 9.0%; $p<0.001$) and fewer pts had radiographic erosions (58.2 vs 71.5%; $p<0.001$) for biologic-naïve vs biologic-failure pts. At Yr 2, the overall retention rate was 47.9% (95% CI 45.7, 50.0). The retention rate was higher in biologic-naïve vs biologic-failure pts (54.5 vs 45.2%; $p<0.001$) and in pts with 1 vs ≥2 previous biologics (Fig). Reasons for discontinuation were comparable between groups; main reasons were lack of efficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). RF and anti-citrullinated protein antibody (ACPA) seropositivity were prognostic factors for higher retention in biologic-naïve (p=0.030) and biologic-failure pts (p=0.028); other positively impacting factors were diabetes mellitus (p=0.044; biologic naïve); geographic location ($p<0.001$; biologic naïve) and ABA combination therapy ($p<0.001$; biologic failure). Only Pt Global Assessment (p=0.009; biologic failure) predicted lower retention. Among pts continuing ABA, a greater proportion of biologic-naïve vs biologic-failure pts had a good/moderate EULAR response (90.7 vs 81.6%; p=0.005) and RF/ACPA seropositivity was associated with a better response (p=0.002). There were no new safety signals.



Conclusions: In this first prospective, international, non-interventional research evaluating the long-term IV abatacept retention, RF and ACPA seropositivity were predictors of 2-yr higher retention and better outcomes. Higher retention rates may be achievable with earlier vs later initiation of abatacept treatment, consistent with prior findings from a pooled analysis of EU and Canadian registries.[1]

References:

[1] Iannone F et al. Clin Rheumatol (2016): doi:10.1007/s10067–016–3505–5.

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FRI0246 IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE WITH SIRUKUMAB ARE STATISTICALLY SIGNIFICANT, CLINICALLY MEANINGFUL, AND MEET OR EXCEED NORMATIVE VALUES IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: POST HOC ANALYSES OF A PHASE 3 TRIAL

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Background: Rheumatoid arthritis (RA) is associated with impaired health-related quality of life (HRQoL). Sirukumab (SIR) is an anti–interleukin-6 (IL-6) monoclonal antibody.

Objectives: These post hoc analyses evaluated improvements in HRQoL compared with an age/gender-matched normative population in a phase 3 randomized, controlled trial of SIR in RA pts with inadequate response to conventional disease-modifying antirheumatic drugs (DMARD-IR; SIRROUND-D).

Methods: 1670 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being was measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (FACIT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).

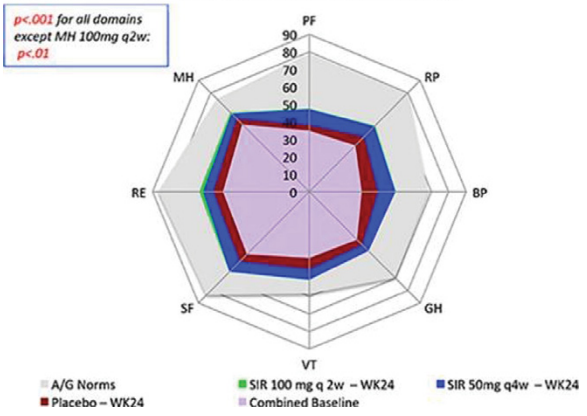
Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL were comparable for pbo, SIR 50mg q4w and 100mg q2w (PCS: 33.8, 34.2, and 33.5; MCS: 40.5, 40.5, and 41.8) and indicative of substantial impairment. At Wk 24, treatment with SIR 50mg q4w and 100mg q2w resulted in significantly greater mean improvements from BL vs pbo in SF-36 PCS (5.4 and 5.9 vs 2.3) and MCS (4.9 and 4.2 vs 2.9) scores (all $P<0.001$), exceeding the minimum clinically important difference (MCID) of 2.5. Least squares mean changes in all SF-36 domain raw scores were significantly greater with both doses of SIR than pbo at Wk 24 and all >MCID of 5.0 (Table; Figure). Substantial proportions of pts treated with SIR 50mg q4w or 100mg q2w reported scores ≥normative values in SF-36 domains at Wk 24 (ranges: 20–33% and 21–36%) vs pbo (range: 10–28%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACIT-F scores were 27.2, 27.1, and 27.5. Significantly greater proportions of pts reported clinically meaningful improvements in FACIT-F (MCID=4) with SIR 50mg q4w and 100mg q2w vs pbo (61.4 and 59.4% vs 43.9%; $P<0.001$). FACIT-F scores ≥normative values were reported by 33% of pts on SIR 50mg q4w and 100mg q2w vs 22% on pbo. HAQ-DI scores at BL were 1.56, 1.50, and 1.52 with pbo, SIR 50mg q4w, and 100mg q2w, with clinically meaningful improvements (MCID= -0.22) reported by 63.0 and 65.4% with SIR 50mg q4w and 100mg q2w vs 46.9% with pbo ($P<0.001$). HAQ-DI scores ≥normative values were reported by numerically more pts receiving SIR 50mg q4w (22%) and 100mg q2w (21%) vs pbo (10%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all $P \leq 0.006$)

Domain	LSM change SIR 50mg q4w	LSM change SIR 100mg q2w	LSM change pbo
Physical function	10.48	12.39	2.85
Role-physical	14.88	16.04	7.96
Bodily pain	19.09	18.98	9.44
General health	8.90	7.53	3.57
Vitality	11.83	11.96	6.37
Social function	13.49	13.25	7.65
Role-emotional	12.50	11.74	6.54
Mental health	9.26	7.97	5.00

LSM, least squares mean.

Figure. SF-36 domains at Wk 24 for SIR 50mg q4w and SIR 100mg q2w



Conclusions: Through 24 wks, SIR treatment resulted in greater improvements in HRQoL than pbo that were clinically meaningful and met or exceeded normative values in DMARD-IR RA pts, with similar effects observed with both doses of SIR.

Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK,