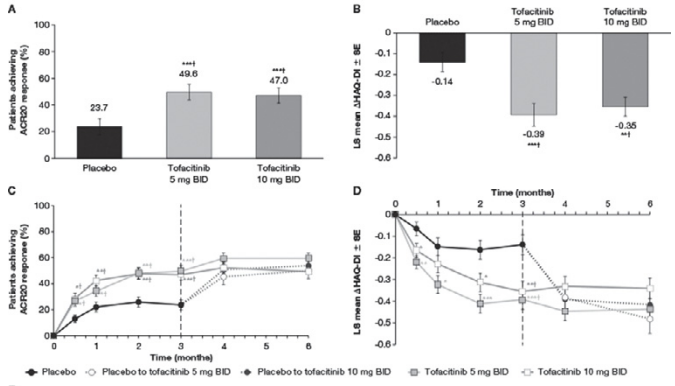
28.8% [p≤0.05] vs 13.0%). Secondary endpoints at M3 for tofacitinib 5 mg and 10 mg respectively were: ACR50 response, 29.8% (p≤0.05), 28.0% (p≤0.05); ACR70 response, 16.8% (not significant [NS]), 14.4% (NS); ≥75% improvement of PASI in pts with baseline BSA ≥3% and PASI >0, 21.3% (NS), 43.2% (p<0.0001); ΔLEI and ΔDSS in pts with baseline score >0: ΔLEI, -1.3 (p≤0.05) and -1.3 (p≤0.05) (least squares mean [LSM]); ΔDSS, -5.2 (p≤0.05) and -5.4 (p≤0.05) (LSM). Effects were maintained to M6. Frequency of serious AEs and discontinuations due to AEs was low and similar across treatment groups (Fig 1E). The most common AEs were upper respiratory tract infection (5.3–10.8%), nasopharyngitis (1.5–10.7%) and headache (4.5–9.1%).

Figure 1. A. ACR20 response rates with tofacitinib vs placebo at M3, B. ΔHAQ-DI with tofacitinib vs placebo at M3, C. ACR20 response rates up to M6, D. ΔHAQ-DI up to M6, E. Safety summary (safety analysis set;[a] all causality)



E

	Up to M3	Up to M6			
	Placebo (N=131)	Placebo → tofacitinib 5 mg BID (N=66)	Placebo → tofacitinib 10 mg BID (N=65)	Tofacitinib 5 mg BID (N=131)	Tofacitinib 10 mg BID (N=132)
AEs, n (%)	58 (44.3)	40 (60.6)	38 (58.5)	93 (71.0)	96 (72.7)
SAEs, n (%)	3 (2.3)	2 (3.0)	1 (1.5)	5 (3.8)	8 (6.1)
Discontinuation due to AEs, n (%)	5 (3.8)	2 (3.0)	3 (4.6)	5 (3.8)	11 (8.3)
Deathe, n (%)	0	0	0	0	0
AEs of special interest, n (%) [day of onset]					
Serious infection	0	0	0	2 (1.5) [135, 166]	2 (1.5) [10, 69]
Herpes zoster (all non-serious)	0	0	0	1 (0.8) [77]	2 (1.5) [8, 156]
Malignancy[b]	0	0	0	0	0
MACE[c]	0	0	0	1 (0.8) [245]	1 (0.8) [94]

Nominal *p≤0.05, **p<0.001, ***p<0.0001 vs placebo; [a]Achieved statistical significance at p≤0.05 per the pre-specified step-down testing procedure; dashed line indicates the end of the placebo-controlled period; [b]All patients who received ≥1 dose of study medication; [c]Including non-melanoma skin cancer; [d]For this trial, MACE included one myocardial infarction and one cerebrovascular event (stroke)
ACR, American College of Rheumatology; AE, adverse event; BID, twice daily; HAQ-DI, Health Assessment Questionnaire-Disability Index; M, month; MACE, major adverse cardiovascular event; n, number of patients with event; SAE, serious adverse event; SE, standard error

Conclusions: In this study restricted to PsA pts with TNFi-IR, both tofacitinib doses appeared efficacious on musculoskeletal endpoints for treatment of PsA. No new safety risks were identified vs previous studies in other indications.

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Immunogenicity of biologics; myth or reality?

OP0203 IMPACT OF ADALIMUMAB SERUM CONCENTRATION ON EFFICACY AND ASSOCIATION BETWEEN ANTI-DRUG ANTIBODIES AND SERUM CONCENTRATION: 24 WEEK RESULTS FROM A PHASE III STUDY COMPARING SB5 (AN ADALIMUMAB BIOSIMILAR) WITH REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SB5 has been developed as a biosimilar of reference adalimumab (ADL). The 24-week efficacy and safety results comparing SB5 and ADL were reported previously.[1] Here we report results of subgroup analyses of efficacy by adalimumab serum trough concentration (C_{trough}) and association between anti-drug antibodies (ADA) and C_{trough}.

Objectives: To investigate the impact of C_{trough} on efficacy and the association between ADA and C_{trough} in patients with rheumatoid arthritis (RA) treated with SB5 or ADL.

Methods: Patients with moderate to severe RA despite methotrexate treatment were randomly assigned to receive 40 mg of either SB5 or ADL administered subcutaneously every other week up to week 24. Blood samples were taken prior to study drug administration at weeks 0, 4, 8, 12, 16, and 24 to measure C_{trough}. The optimal C_{trough} cut-off point of adalimumab for good EULAR response at week 24 is reported to be 1.274 μg/mL.[2] Efficacy and immunogenicity were analysed in patients with C_{trough} <1.274 μg/mL and ≥1.274 μg/mL.

Results: C_{trough} was measured in 178 patients each from SB5 and ADL group. The post-dose mean C_{trough} was comparable up to week 24 for SB5 (range: 3.850 to 6.761 μg/mL) and ADL (range: 3.892 to 6.773 μg/mL). Generally, efficacy was higher in patients with C_{trough} ≥1.274 μg/mL for both SB5 and ADL but it was comparable between SB5 and ADL regardless of C_{trough} level. At week 24, the proportion of patients achieving good EULAR response, remission or low disease activity based on DAS28 was higher in patients with C_{trough} ≥1.274 μg/mL than in those with C_{trough} <1.274 μg/mL for both treatment groups (Figure). Other efficacy parameters, including ACR responses, DAS28, simplified disease activity index, and clinical disease activity index, showed similar results.

C_{trough} was higher for patients without detectable ADA, compared to those with ADA. Among patients with ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 58.0% (29/50) for SB5 and 52.1% (25/48) for ADL. Among patients without detectable ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 100.0% (121/121) for SB5 and 97.4% (114/117) for ADL.

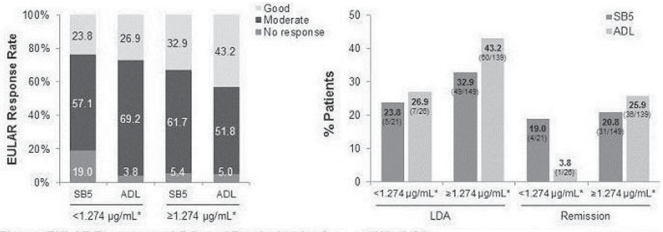

Figure. EULAR Responses, LDA, and Remission by C_{trough} at Week 24
*C_{trough} level; LDA, low disease activity
LDA defined as DAS28 ≤ 3.2 and remission defined as DAS28 < 2.6.

Conclusions: The presence of ADA reduces C_{trough} for both SB5 and ADL. In both treatment groups, almost all patients without detectable ADA, but only slightly more than half of patients with ADA, had C_{trough} ≥1.274 μg/mL at week 24. Efficacy and ADA incidence were generally comparable between SB5 and ADL regardless of C_{trough} level. However, patients with C_{trough} ≥1.274 μg/mL generally experienced greater efficacy of both SB5 and ADL than that in patients with C_{trough} <1.274 μg/mL.

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[1] Weinblatt ME et al. Arthritis Rheumatol. 2015; 67 (suppl 10), 8L.
[2] Chen DY et al., Ann Rheum Dis. 2015; Mar;74(3):e16.

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