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SAT0069 A RAPID3-LIKE INDEX DOCUMENTS SUPERIOR EFFICACY OF BARICITINIB TO ADALIMUMAB AND PLACEBO, SIMILAR TO DAS28 AND CDAI IN THE RA-BEAM CLINICAL TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: RAPID3 (Routine Assessment of Patient Index Data) indicates differences in efficacy of active versus control treatments at levels similar to DAS28-ESR (Disease Activity Score 28-Erythrocyte Sedimentation Rate) and CDAI (Clinical Disease Activity Index) in clinical trials of adalimumab, abatacept, certolizumab.
Objectives: To compare improvement according to RAPID3, DAS 28-ESR, and CDAI in the RA-BEAM trial of baricitinib vs adalimumab and placebo.
Methods: Post-hoc analyses were performed of the RA-BEAM trial, in which patients with moderately to severely active rheumatoid arthritis and an inadequate response to methotrexate (MTX) were randomized to baricitinib, adalimumab, or placebo. All patients were to continue stable background MTX and other DMARDs, as well as stable low-dose prednisone and/or NSAIDs, if indicated. A RAPID3-like index was computed from 3 measures: physical function (FN), pain (PN), and patient global assessment (PATGL). FN on a HAQ (Health Assessment Questionnaire) of 20 items [rather than MDHAQ (multidimensional HAQ) of 10 items] was recalculated from 0–3 to 0–10; PN and PATGL (visual analog scales) were recalculated from 0–100 to 0–10, for a 0–30 total score, hence “RAPID3-like”. Mean values at baseline and Week 24 for RAPID3-like, DAS28-ESR, and CDAI, and percent change from baseline were computed in the 3 treatment groups. The proportion of patients with high/moderate activity/severity at Week 24 versus low activity/severity/remission, as well as correlations of the 3 indices at Week 24, were calculated. Statistical significance for percent change was analyzed using Wilcoxon tests, after imputation of missing values using modified last observation carried forward (mLOCF); low activity/severity/remission was compared between groups using a logistic model, adjusting for region and baseline joint erosion status after imputation of missing values using non-responder imputation.
Results: Improvement from baseline to Week 24 ranged from 19.2% to 37.0% in placebo patients, 40.0% to 65.9% in baricitinib-treated patients, and 37.6% to 60.9% in adalimumab-treated patients (Table), least in DAS28-ESR, intermediate in RAPID3-like, and highest in CDAI. Changes according to RAPID3-like, DAS28-ESR and CDAI were similar in the 3 treatment groups; baricitinib and adalimumab were superior to placebo according to all indices, and baricitinib was superior to adalimumab according to RAPID3-like and CDAI (Table). Correlations of RAPID3-like with DAS28-ESR and CDAI ranged from r=0.61 to 0.75 and for DAS28-ESR with CDAI from r=0.86 to 0.91 (all p<0.001). The proportion of patients with low activity/severity/remission at Week 24 ranged from 9.6% to 19.7% in placebo patients, 31.6% to 49.9% in baricitinib-treated patients, and 33.6% to 47.6% in adalimumab-treated patients. RAPID3-like results were intermediate between DAS28-ESR and CDAI.

Table. Disease Activity/Severity by 3 Indices through Week 24 in RA-BEAM

	Baseline Mean	Week 24 Mean	% Change from Baseline	Correlation with DAS28-ESR	Correlation with CDAI	High or Mod at Week 24 n (%)	Low or Remission at Week 24 n (%)
RAPID3-like							
Placebo (N=488)	17.2	12.7	-22.5%	0.69	0.61	399 (81.8%)	89 (18.2%)
Baricitinib (N=487)	17.7	8.4	-51.0%***	0.67	0.63	266 (54.6%)	221 (45.4%)*
Adalimumab (N=330)	17.8	9.6	-45.6%***	0.75	0.70	217 (65.8%)	113 (34.2%)*
All (N=1305)				0.73	0.67		
DAS28-ESR							
Placebo (N=488)	6.4	5.2	-19.2%	N/A	0.91	441 (90.4%)	47 (9.6%)
Baricitinib (N=487)	6.5	3.9	-40.0%***	N/A	0.86	333 (68.4%)	154 (31.6%)*
Adalimumab (N=330)	6.4	4.0	-37.6%***	N/A	0.87	219 (66.4%)	111 (33.6%)*
All (N=1305)				N/A	0.90		
CDAI							
Placebo (N=488)	37.6	23.4	-37.0%	0.91	N/A	392 (80.3%)	96 (19.7%)
Baricitinib (N=487)	38.1	13.0	-65.9%***	0.86	N/A	244 (50.1%)	243 (49.9%)*
Adalimumab (N=330)	38.0	15.0	-60.9%***	0.87	N/A	173 (52.4%)	157 (47.6%)*
All (N=1305)				0.90	N/A		

***Significant at 0.001 level, Baricitinib or Adalimumab vs. Placebo.
*, *Significant at 0.01 and 0.05 levels respectively, Baricitinib vs. Adalimumab.
Abbreviations: CDAI=Clinical Disease Activity Index; DAS28-ESR=Disease Activity Score 28-erythrocyte sedimentation rate; High=high disease activity/severity; Low=low disease activity/severity; Mod=moderate disease activity/severity; N=number of patients; RAPID3-like=Routine Assessment of Patient Index Data 3-like.

Conclusions: RAPID3-like documented greater efficacy of baricitinib versus adalimumab and placebo in the RA-BEAM trial, with results in similar ranges to DAS28-ESR and CDAI. RAPID3 is feasible to provide quantitative, standard medical history data; almost of the time and effort is by the patient rather than a health professional, assuring quantitative data in the infrastructure of usual clinical care.

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SAT0070 BARICITINIB VERSUS ADALIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: ANALYSIS OF PATIENTS ACHIEVING A MODERATE EULAR RESPONSE AT WEEK 4

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Background: Baricitinib (BARI) is a selective inhibitor of Janus kinase,¹ improves disease activity in patients (pts) with rheumatoid arthritis (RA), and is associated with inhibition of structural joint damage.^{2–4} Response to BARI observed at week (wk) 4 may be useful to predict future response.⁵
Objectives: To characterise pts with RA who achieved moderate EULAR responses (MERs)⁶ at wk 4 and to describe the outcomes through wk 52 while continuing the assigned treatment.
Methods: Pts enrolled in the RA-BEAM study with active RA who had an inadequate response to methotrexate (MTX) were randomised 3:3:2 to placebo (PBO), BARI 4 mg once daily, or adalimumab (ADA) 40 mg biweekly.¹ Pts who showed good or no EULAR responses at wk 4 were excluded. For the MER cohort, the cumulative incidence for first transition to good EULAR response and to no EULAR response from wk 4 through wk 52 was estimated in the presence of competing risks events, which either hinder observation of the events of interest or modify the chance that these events occur.⁷ Pts who transitioned from MER to no EULAR response or pts who were rescued or discontinued because of an adverse event or lack of efficacy were counted as no EULAR response; pts who discontinued the study for other reasons (eg, lost to follow-up, death) were censored at the time of discontinuation. No formal statistical tests were performed for these post hoc analyses.
Results: Of 1305 pts who received at least 1 dose of study drug, 683 experienced MERs at wk 4, including 37.3% (182/488), 62.0% (302/487), and 60.3% (199/330) of pts on PBO, BARI, and ADA, respectively. Pts who achieved MERs at wk 4 on BARI and ADA had similar baseline disease activity characteristics (Table 1). The mean age of the MER subgroup was 53 years, and the mean disease duration was 8.7 years. The mean MTX dosage was 15 mg/wk, and 59% of pts were taking concomitant oral glucocorticoids. At wk 4, 27% (131/487) and 11% (54/487) of pts on BARI vs 29% (95/330) and 11% (36/330) of pts on ADA experienced no response or good response, respectively. The cumulative incidence for the first transitions to good EULAR response at wks 12, 24, and 52 was higher in pts who reached MERs at wk 4 on BARI than those on ADA. The cumulative incidence for the first transitions to subsequent no EULAR response was higher in pts who achieved MER at wk 4 on ADA (Figures 1A and 1B, Table 2) than those on BARI.
Conclusions: Among pts achieving early MER on BARI and ADA, subsequent loss of response was less common for pts on BARI than for those on ADA. Transitions to good EULAR response were more common for pts who achieved MERs on BARI than for those on ADA. Mechanistic explanations warrant future study.

Table 1: Baseline Characteristics for Patients with Moderate EULAR Response at Week 4

Characteristic	Baricitinib n = 302*	Adalimumab n = 199*
Background therapy (MTX only), no. (%)	259 (85.8)	173 (86.9)
Background therapy (MTX + other cDMARD), no. (%)	43 (14.2)	26 (13.1)
DAS28-ESR, mean (SD)	6.6 (0.9)	6.5 (0.9)
DAS28-ESR category, no. (%)		
>3.2 to ≤5.1	12 (4.0)	8 (4.0)
≤5.1	290 (96.0)	191 (96.0)
Baseline mTSS, mean (SD)	42.0 (50.0)	47.1 (51.9)
HAQ-DI total score, mean (SD)	1.6 (0.7)	1.6 (0.7)

Abbreviations: cDMARD=conventional disease-modifying antirheumatic drug; DAS28-ESR=Disease Activity Score modified to include the 28-joint count based on the erythrocyte sedimentation rate; HAQ-DI=Health Assessment Questionnaire-Disability Index; mTSS=modified Total Sharp Score; MTX=methotrexate.
*501 patients reached moderate EULAR response at week 4: 302/487 (62%) and 199/330 (60%) for BARI and ADA, respectively.

Table 2: Time to First Transition to Good and to No EULAR Response (DAS28-ESR)

	Baricitinib			Adalimumab		
	Cumulative Incidence (%)	Lower	Upper	Cumulative Incidence (%)	Lower	Upper
Transition to Good Response						
Week 12	18.3	14.1	22.8	15.2	10.6	20.5
Week 24	49.2	43.4	54.7	42.9	35.9	49.7
Week 52	63.6	57.8	68.8	58.1	50.9	64.7
Transition to No Response						
Week 12	8.6	5.8	12.2	13.2	8.9	18.3
Week 24	18.9	14.7	23.5	25.5	19.6	31.7
Week 52	24.2	19.5	29.2	28.9	22.7	35.4

Abbreviations: CI=confidence interval; DAS28-ESR=Disease Activity Score modified to include the 28-joint count based on the erythrocyte sedimentation rate.

Figure 1: Time until First transition to Good and No EULAR Response (DAS28-ESR)

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SAT0071 RHEUMATOID ARTHRITIS (RA) REGISTRY IN AKITA PREFECTURE, WHERE AGING IS THE MOST ADVANCED IN JAPAN

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Background: The rate of aging (percentage of population aged 65 years and over) in Akita Prefecture is 33.8% (26.6% for the whole of Japan), the highest throughout Japan. The Akita Orthopaedic Group on Rheumatoid Arthritis (AORA) was established in 2010. Since then, patients have been enrolled every year to prepare the registry.

Objectives: To compare patient characteristics as well as clinical effectiveness between the treatments with and without use of methotrexate (MTX) and a biological (BIO) using the data of the AORA registry.

Methods: The subjects were 2,016 patients enrolled in the Akita registry in 2015. The subjects included 403 men and 1,613 women. According to the use of MTX and BIO, 2,016 patients were divided into the group treated with no use of MTX or BIO (group A), that treated with BIO, but no use of MTX (group B), that treated with MTX, but no use of BIO (group C), and that treated with MTX and BIO (group D).

Abstract SAT0072 – Table 1

Pts originating from RA-BEAM, RA-BUILD, RA-BEACON Combined†						
	Week 12		Week 24		Week 48	
	Continued bari 4 mg N=396	Stepped down to bari 2 mg N=394	Continued bari 4 mg N=353	Stepped down to bari 2 mg N=358	Continued bari 4 mg N=245	Stepped down to bari 2 mg N=245
Efficacy measure	NRI after rescue or for missing data					
CDAI LDA ≤10	359/396 (90.7)	326/393 (83.0)**	309/353 (87.5)	269/357 (75.4)***	198/245 (80.8)	167/245 (68.2)**
CDAI remission ≤2.8	158/396 (39.9)	143/393 (36.4)	149/353 (42.2)	127/357 (35.6)	99/245 (40.4)	82/245 (33.5)
	NRI only for missing data (observed data used after rescue)					
CDAI LDA ≤10	359/396 (90.7)	326/393 (83.0)**	314/353 (89.0)	289/357 (81.0)**	212/245 (86.5)	196/245 (80.0)
CDAI remission ≤2.8	158/396 (39.9)	143/393 (36.4)	150/353 (42.5)	133/357 (37.3)	103/245 (42.0)	90/245 (36.7)
Safety measure	Wks 0–48					
n [EAIR/100 PYE]	Continued bari 4mg N=396			Stepped down to bari 2mg N=394		
SDEAE	225 [70.5]			196 [65.4]		
Infection	99 [31.0]			70 [23.3]		
SAE	23 [7.2]			23 [7.7]		
Serious infection	8 [2.5]			4 [1.3]		
AE → discontinuation	9 [2.8]			11 [3.6]		

Efficacy and safety data are n/N (%), and n [EAIR/100 PYE], respectively. †RA-BEAM = MTX-IR pts; RA-BUILD = csDMARD-IR pts; RA-BEACON = bDMARD-IR pts; EAIR = exposure-adjusted incidence rate; NRI = nonresponder imputation; PYE = patient-years of exposure; SDEAE = step-down emergent adverse event. **p<0.01, ***p<0.001 vs. continued bari 4mg.

Results: The subjects were grouped into group A (n=673), B (n=153), C (n=805), and D (n=385). MTX was used in 59.0% and BIO was used in 26.7% of all patients. The mean ages were 69.6 years (group A), 65.7 years (group B), 65.6 years (group C), and 62.6 years (group D). The aging rates were 67.9% (group A), 55.6% (group B), 56.8% (group C), and 48.3% (group D), which shows that aging was more advanced in group A.

The rates of patients with a complication of hypertension, diabetes, respiratory disease, cerebrovascular disease, heart disease or malignant tumour were 52.0% (group A), 54.2% (group B), 45.5% (group C), and 40.8% (group D). The incidence of complication was the lowest in group D.

The rates of patients who received one or more of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) other than MTX were 79.0% (group A), 42.5% (group B), 39.9% (group C), and 19.2% (group D). Although bucillamine and salazosulfapyridine were frequently used in any group, concomitant use of tacrolimus was remarkable in group A and C, while that of iguratimod was remarkable in groups C and D. The rate of use of a prednisolone (PSL), was significantly higher in group B. The dose of PSL was significantly higher in group A. In regard to BIO, three drugs of etanercept, tocilizumab, and abatacept accounted for 90% in group B. In group D, etanercept and tocilizumab were also frequently used, followed by infliximab, adalimumab, golimumab and abatacept.

In DAS28ESR, the rate of combined low disease activity and remission was significantly higher in group D. The mean values of C-reactive protein (CRP) (mg/dL) were 0.61 (group A), 0.52 (group B), 0.47 (group C), and 0.35 (group D), which shows that the mean value was significantly higher in group A than group D. The mean values of matrix metalloproteinase 3 (MMP3) (ng/dL) were 119.0 (group A), 130.6 (group B), 100.7 (group C), and 88.9 (group D), which shows that the mean value was significantly higher in group A and B than group C and D.

Conclusions: Using the AORA registry, we compared patient characteristics as well as clinical effectiveness between the treatments with and without use of MTX and BIO. Since in group A, neither MTX nor BIO could be used in most patients, one had to practically rely on PSL. The study suggests that remission needs to be achieved prior to increase in complication due to aging.

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SAT0072 DOSE REDUCTION OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING SUSTAINED DISEASE CONTROL: RESULTS OF A PROSPECTIVE STUDY

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Background: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response (IR) to DMARDs, ph3 studies demonstrated efficacy of baricitinib (bari) (2mg and 4mg). Larger, more rapid treatment effects were observed for bari 4mg.

Objectives: To investigate the effects of bari dose step-down in pts who achieved sustained disease control with bari 4mg.

Methods: Pts with RA who completed a bari ph3 study could enter a long-term extension (LTE) study. In the LTE, pts who received bari 4mg for ≥15 months and who achieved sustained low disease activity ([LDA]-CDAI score ≤10) or remission (CDAI ≤2.8) at 2 consecutive visits ≥3 months apart were re-randomised in a blinded manner to continue bari 4mg or step down to 2mg. Patients could rescue (to bari 4mg) if CDAI >10. Efficacy and safety were assessed through 48 weeks (wks) following re-randomisation.

Results: Among pts who achieved sustained disease control with bari 4mg, dose reduction to 2mg resulted in significant increases in disease activity at 12, 24, and 48 wks; however, the majority of pts in both groups maintained the state of LDA