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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.