Efficacy and Safety of Baricitinib Versus Placebo and Adalimumab in Patients with Moderately to Severely Active Rheumatoid Arthritis and Inadequate Response to Methotrexate: Summary Results from the 52-Week Phase 3 RA-Beam Study

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Background: Baricitinib, an oral JAK1/JAK2 inhibitor, has shown promising results in patients with active rheumatoid arthritis (RA). We present efficacy and safety results from the phase 3 RA-BEAM study in patients with active RA and inadequate response (IR) to methotrexate (MTX).

Methods: Patients with moderate to severe RA and MTX-IR were randomized 3:3:2 to placebo, baricitinib 4 mg QD or adalimumab 40 mg biweekly. All patients continued stable background MTX therapy. Non-responders were rescued at week 16. At week 24, patients receiving placebo switched to baricitinib 4 mg QD. The study compared baricitinib, placebo and adalimumab using multiple endpoints, including non-inferiority and superiority testing; the primary endpoint was baricitinib versus placebo ACR20 response at week 12.

Results: Of 1305 randomized patients, 83%, 88% and 87% completed week 52 in the placebo, baricitinib and adalimumab groups, respectively; rescue rates were 27%, 9% and 15%, respectively. ACR20 response at week 12 was higher for baricitinib versus placebo ($p \leq .001$; Table 1). At weeks 12 and 24, significant improvements were seen for baricitinib versus placebo in ACR20/50/70 and DAS28, CDAI and SDAI low disease activity and remission rates, many by week one. Baricitinib was

superior to adalimumab in ACR20 response rates at weeks 12, 24 and 52, and in DAS28-CRP≤3.2 at weeks 12 and 52. Change in mTSS at weeks 24 and 52 was significantly lower for baricitinib versus placebo (Table). At week 24, more baricitinib patients had improved physical function and reduced fatigue and pain versus placebo and adalimumab (Table). During weeks 0–24, more treatment-emergent AEs occurred with baricitinib and adalimumab versus placebo (71%, 67%, 60%); serious AE rates were 5%, 2% and 4%, respectively. By week 52, treatment-emergent AE rates for baricitinib versus adalimumab were 79% versus 77% and serious AE rates were 8% versus 4%; serious infection rates were similar across groups; three major cardiovascular events (2 baricitinib, 1 adalimumab), three deaths (2 baricitinib, 1 adalimumab), one tuberculosis case (adalimumab), and five malignancies (2 baricitinib, 3 placebo) were reported.

Conclusion: In patients with moderate to severe RA and MTX-IR receiving background MTX, addition of baricitinib was associated with significant clinical improvements versus placebo and adalimumab, with an acceptable safety profile.

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Table.

RA-BEAM efficacy measures up to week 52

	Week 12			Week 24			Week 52	
	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	Bari (n = 487)	ADA (n = 330)
ACR20	40	70***+	61***	37	74***+	66***	71++	62
ACR50	17	45***++	35***	19	50***	46***	56++	47
ACR70	5	19***+	13***	8	30***+	22***	37	31
DAS28-CRP ≤3.2	14	44***++	35***	19	52***	48***	56+	48
DAS28-CRP <2.6	4	24***	19***	8	35***	32***	40	39
DAS28-ESR ≤3.2	7	24***	21***	10	32***	34***	39	36
DAS28-ESR <2.6	2	11***	12***	5	18***	18***	23	22
CDAI ≤10	17	40***+	33***	20	50***	48***	57+	49
CDAI ≤2.8	2	8***	7**	4	16***	12***	22	18
SDAI ≤11	16	42***+	35***	20	51***	49***	57+	49
SDAI ≤3.3	2	8***	8***	3	16***	14***	23	18
LS mean ΔmTSSa				0.90	0.41***	0.33***	0.71***	0.60***

	Week 12			Week 24			Week 52	
	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	Bari (n = 487)	ADA (n = 330)
HAQ-DI MCID ≥0.22	58	75***	71***	45	73***+	64***	68++	58
FACIT-F MCID ≥3.56	59	66*	68**	43	65***+	59***	60	54
LS mean ΔDAS28-CRPa	−1.0	−2.2***+++	−1.9***	−1.1	−2.4***+	−2.2***		
LS mean Δpatient's assessment of paina	−17	−32***++	−26***	−18	−34***++	−29***	−36+++	−30
LS mean Δpatient's global assessment of disease activitya	−17	−31***++	−27***	−17	−33***+	−29***	−36+++	−30

	Week 12			Week 24			Week 52	
	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	Bari (n = 487)	ADA (n = 330)
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ACR50	17	45***++	35***	19	50***	46***	56++	47

	Week 12			Week 24			Week 52	
	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	Bari (n = 487)	ADA (n = 330)
ACR70	5	19***+	13***	8	30***+	22***	37	31
DAS28-CRP ≤3.2	14	44***++	35***	19	52***	48***	56+	48
DAS28-CRP <2.6	4	24***	19***	8	35***	32***	40	39
DAS28-ESR ≤3.2	7	24***	21***	10	32***	34***	39	36
DAS28-ESR <2.6	2	11***	12***	5	18***	18***	23	22
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CDAI ≤2.8	2	8***	7**	4	16***	12***	22	18
SDAI ≤11	16	42***+	35***	20	51***	49***	57+	49
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	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	PBO (n = 488)	Bari (n = 487)	ADA (n = 330)	Bari (n = 487)	ADA (n = 330)
LS mean ΔDAS28-CRPa	−1.0	−2.2***+++	−1.9***	−1.1	−2.4***+	−2.2***		
LS mean Δpatient's assessment of paina	−17	−32***++	−26***	−18	−34***++	−29***	−36+++	−30
LS mean Δpatient's global assessment of disease activitya	−17	−31***++	−27***	−17	−33***+	−29***	−36+++	−30

PBO, placebo; Bari, baricitinib; ADA, adalimumab; mTSS, modified total Sharp score; MCID, minimal clinically important difference.

Patients received stable background MTX throughout the study. Data are % patients (non-responder imputation), unless otherwise stated.

A Data are least square (LS) mean change from baseline;

* p≤0.05,

** p≤0.01,

*** p≤0.001 vs PBO;

+ p≤0.05,

++ p≤0.01,

+++ p≤0.001 vs ADA