

## Online Supplement

**Table S1. Patient characteristics, disease activity and patient-reported outcomes (PROs) at baseline**

Parameter*	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=177)
<b><i>Patient characteristics</i></b>			
Age, years	56 (11)	55 (11)	56 (11)
Female patients, n (%)	145 (82)	137 (79)	149 (84)
Duration of RA time from symptom onset, years	14 (10)	14 (8)	14 (9)
time from diagnosis, years	13 (9)	12 (8)	12 (9)
Number of prior csDMARDs, n (%)			
0	0	0	1 (1)
1	75 (43)	66 (38)	71 (40)
2	47 (27)	54 (31)	52 (29)
≥3	54 (31)	54 (31)	53 (30)
Number of prior bDMARDs <sup>+</sup> , n (%)			
1	81 (46)	69 (40)	71 (40)
2	47 (27)	55 (32)	58 (33)
≥3	47 (27)	50 (29)	45 (25)
TNFi <sup>‡</sup>			
1	104 (59)	102 (59)	104 (59)
2	50 (28)	60 (34)	52 (29)
≥3	19 (11)	12 (7)	18 (10)
Non-TNFi			
1	37 (21)	45 (26)	43 (24)
2	15 (9)	14 (8)	14 (8)
≥3	10 (6)	11 (6)	10 (6)

<b>Parameter*</b>	<b>Placebo (N=176)</b>	<b>Baricitinib 2 mg (N=174)</b>	<b>Baricitinib 4 mg (N=177)</b>
<b><i>Disease activity</i></b>			
Swollen joint count, of 66	17 (11)	19 (12)	16 (9)
Tender joint count, of 68	28 (16)	31 (16)	28 (16)
hsCRP, mg/L (ULN = 3 mg/L)	21 (25)	20 (22)	20 (25)
ESR, mm/hour	47 (24)	45 (24)	48 (26)
DAS28-hsCRP	5.9 (0.9)	6.0 (0.9)	5.9 (1.0)
CDAI	41 (13)	43 (13)	40 (14)
SDAI	43 (14)	45 (14)	42 (14)
<b><i>Patient-reported outcome measures</i></b>			
HRQOL (SF-36; 0–100)			
PCS	28.2 (7.7)	28.7 (8.1)	29.5 (9.0)
MCS	46.1 (13.7)	46.1 (13.1)	46.0 (13.0)
EQ-5D-5L			
Health State Index Score, UK algorithm (-0.594–1)	0.443 (0.250)	0.461 (0.233)	0.427 (0.260)
Self-perceived health score VAS (0–100)	47.8 (22.4)	46.0 (20.8)	47.4 (24.3)
Fatigue (FACIT-F; 0–52)	22.2 (10.6)	22.5 (10.0)	23.4 (11.3)
HAQ-DI (0–3)	1.78 (0.57)	1.71 (0.55)	1.74 (0.59)
PtGA (0–100 VAS)	66 (19)	67 (19)	66 (22)
Patient's assessment of pain (0–100 VAS)	65 (19)	62 (22)	66 (23)
Median (IQR) duration of morning joint stiffness, minutes	90.0 (30.0, 150.0)	91.0 (40.0, 180.0)	90.0 (30.0, 180.0)
Worst Joint Pain NRS (0– 10)	7.2 (1.8)	7.1 (1.7)	7.1 (2.0)

<b>Parameter*</b>	<b>Placebo (N=176)</b>	<b>Baricitinib 2 mg (N=174)</b>	<b>Baricitinib 4 mg (N=177)</b>
Worst Tiredness NRS (0–10)	6.9 (2.1)	7.2 (1.8)	6.9 (2.2)

\*Data are presented as mean (standard deviation) unless stated otherwise. Additional data on the patient baseline characteristics can be found in Genovese et al. [17]

\*4 patients (0.8%) did not receive any prior bDMARDs

‡This group includes both patients who have taken only 1 TNFi and those who have taken a combination of 1 TNFi and any other non-TNFi agents. These patients, therefore, may be taking multiple b-DMARDs; as such, this group is not a subset of the bDMARD = 1 group.

bDMARDs = biological disease-modifying antirheumatic drugs; CDAI: Clinical Disease Activity Index; csDMARDs = conventional synthetic disease-modifying antirheumatic drugs;; DAS = Disease Activity Score; EQ-5D-5L = European Quality of Life-5 Dimensions-5 Levels; ESR = erythrocyte sedimentation rate; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI = Health Assessment Questionnaire-Disability Index; hsCRP = high-sensitivity C-reactive protein; IQR = interquartile range; MCS = mental component score; NRS = Numeric Rating Scale; PCS = physical component score; PtGA = Patient's Global Assessment of Disease Activity; HRQOL = health-related quality of life; RA = rheumatoid arthritis; SF-36 = Short Form 36 Health Survey; SDAI: Simple Disease Activity Index ; TNFi = tumour necrosis factor inhibitor; UK = United Kingdom; ULN = upper limit of normal; VAS = visual analogue scale.

Score ranges for individual PRO measures are indicated in brackets in the left hand column. Lower scores indicate better outcomes for HAQ-DI, PtGA, patient's assessment of pain, Worst Joint Pain, Worst Tiredness. Higher scores indicate better outcomes for SF-36, EQ-5D and FACIT-F.

**Table S2. Baseline values and least squares mean change from baseline at Weeks 12 and 24 for SF-36 domain scores**

SF-36 domain scores	Baseline mean (SD)			Week 12 LSM Δ from baseline			Week 24 LSM Δ from baseline		
	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=177)	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=177)	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=177)
Physical functioning	27.8 (8.7)	29.2 (9.1)	29.3 (10.0)	1.4	5.2***	4.7***	0.7	5.6***	5.6***
Role physical	32.4 (9.4)	33.0 (8.8)	33.9 (9.6)	2.9	5.7**	5.1*	2.3	5.5***	5.8***
Bodily pain	31.3 (7.2)	32.2 (6.7)	32.0 (7.8)	4.0	7.4***	8.2***	3.7	7.1***	9.2***
General health	36.4 (8.5)	35.2 (9.3)	36.7 (9.2)	1.3	4.0***	3.0*	0.9	3.4**	2.8*
Vitality	38.8 (9.9)	37.7 (10.2)	39.7 (10.6)	3.1	5.6*	5.9**	3.9	6.3*	6.9**
Social functioning	37.8 (11.8)	39.1 (12.1)	37.8 (11.6)	0.9	3.5*	4.2**	1.1	4.2**	5.3***
Role emotional	40.6 (13.9)	42.1 (12.7)	41.7 (13.0)	1.3	4.2**	1.5	1.0	3.6*	2.6
Mental health	43.0 (12.8)	42.9 (12.2)	42.9 (12.5)	1.3	3.4*	2.6	2.1	2.8	3.0

\*p≤0.05, \*\*p≤0.01, \*\*\*p≤0.001 vs. placebo

**Table S3. Percentage of patients achieving MCID  $\geq 2.5$  for the physical and mental component scores (PCS and MCS) of the SF-36**

Week	% of patients achieving MCID $\geq 2.5$					
	4	8	12	16	20	24
<b>Physical Component Score</b>						
Placebo (N=176)	45	49	48	40	51	49
Baricitinib 2 mg (N=174)	59**	63*	63**	63***	63**	64**
Baricitinib 4 mg (N=177)	64***	64**	64***	62***	62**	64***
<b>Mental Component Score</b>						
Placebo (N=176)	36	34	40	36	44	45
Baricitinib 2 mg (N=174)	39	37	46	38	36	44
Baricitinib 4 mg (N=177)	47*	41	44	38	44	44

\* $p \leq 0.05$ , \*\* $p \leq 0.01$ , \*\*\* $p \leq 0.001$  vs. placebo

**Table S4. Work Productivity and Activity Impairment Questionnaire- Rheumatoid Arthritis (WPAI-RA) at baseline and least squares change from baseline at 12 and 24 weeks**

**Table S4A) Mean daily activity impairment due to RA administered to all patients at baseline and LSM change from baseline at Week 12 or 24**

WPAI-RA	Baseline, mean (SD)			Week 12, LSM (95% CI) $\Delta$ from baseline			Week 24, LSM (95% CI) $\Delta$ from baseline		
	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=176)	Placebo (N=157)	Baricitinib 2 mg (N=162)	Baricitinib 4 mg (N=165)	Placebo (N=91)	Baricitinib 2 mg (N=119)	Baricitinib 4 mg (N=125)
Question administered to all patients at given timepoint									
Percentage activity impairment due to RA	66.5 (21.4)	64.0 (19.6)	64.6 (23.1)	-9.5 (-13.6, -5.3)	-16.7** (-20.8, -12.6)	-18.1*** (-22.2-14.0)	-15.2 (-20.8, -9.6)	-22.2* (-27.2, -17.2)	-26.3*** (-31.3, -21.4)

**Table S4B): Number (%) of patients who were employed at baseline and at baseline and Week 12 or 24**

Questions administered to patients who were employed	Placebo (N=176)	Baricitinib 2 mg (N=174)	Baricitinib 4 mg (N=176)	Placebo (N=46)	Baricitinib 2 mg (N=65)	Baricitinib 4 mg (N=57)	Placebo (N=27)	Baricitinib 2 mg (N=44)	Baricitinib 4 mg (N=47)
Employed at timepoint <sup>†</sup> , n (%) of patients	53 (30)	69 (40)	60 (34)	42 (91)	61 (94)	51 (90)	22 (82)	38 (86)	42 (89)

**Table S4C): Mean presenteeism, work productivity loss, and absenteeism at baseline and LSM change from baseline at Week 12 or 24**

	Baseline, mean (SD)			Week 12, LSM (95% CI) $\Delta$ from baseline			Week 24, LSM (95% CI) $\Delta$ from baseline		
Percentage impairment while working due to RA (presenteeism)	47.6 (26.2)	47.6 (21.3)	44.6 (29.1)	0.8 (-7.0, 8.5)	-8.1 (-15.0, -1.2)	-7.9 (-15.7, -0.2)	-3.2 (-15.7, 9.4)	-7.6 (-18.4, 3.2)	-11.7 (-22.2, -1.1)

Percentage of overall work impairment due to RA (work productivity loss)	49.7 (26.7)	52.3 (22.8)	49.1 (30.1)	-0.1 (-8.5, 8.4)	-9.3 (-16.8, -1.8)	-9.4 (-17.8, -1.0)	-0.6 (-14.6, 13.4)	-6.3 (-18.3, 5.7)	-8.4 (-20.2, 3.4)
Percentage of work time missed due to RA (absenteeism) <sup>‡</sup>	10.2 (23.3)	13.7 (24.9)	19.0 (29.7)	2.1 (-4.8, 9.0)	-3.6 (-9.7, 2.5)	-1.9 (-8.7, 5.0)	8.0 (-3.1, 19.1)	5.7 (-3.8, 15.2)	6.0 (-3.3, 15.4)

\*p≤0.05, \*\*p≤0.01, \*\*\*p≤0.001 vs. placebo

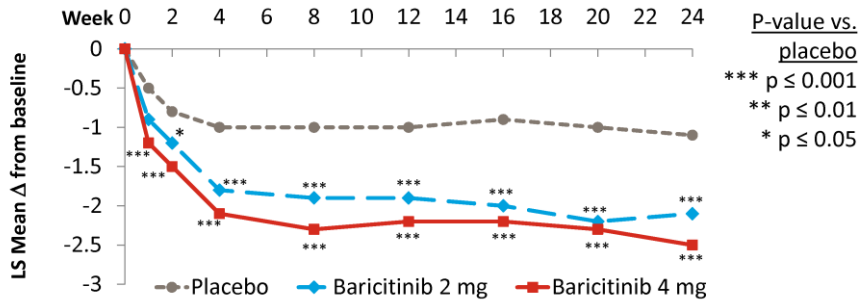
CI = confidence interval; LSM = least squares mean; PtGA = Patient's Global Assessment of Disease Activity; RA = rheumatoid arthritis; SD: Standard Deviation

<sup>†</sup>For Week 12 and 24, % of patients employed at baseline and continued to be employed at the time point

<sup>‡</sup>Results observed at Week 12 for absenteeism were not maintained at Week 24.

**Figure S1. Change in baseline over time for worst joint pain and worst tiredness**

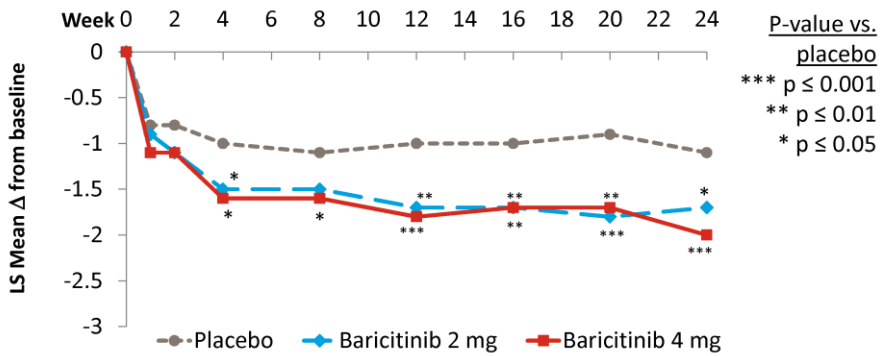
**A) Worst Joint Pain**



Higher scores indicate worse joint pain.

Higher scores indicate worse joint pain.

**B) Worst Tiredness**



Higher scores indicate more tiredness.

Higher scores indicate more tiredness

LS = least squares; MCID = minimum clinically important difference