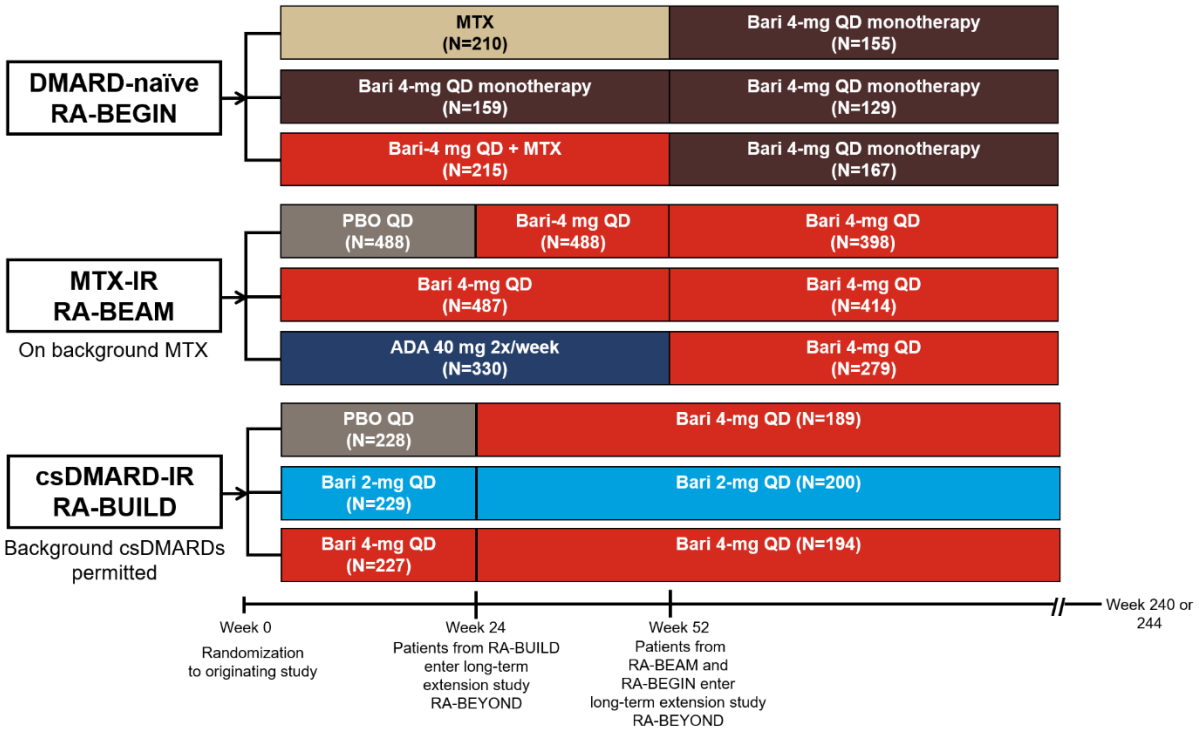
Online supplement to: Radiographic progression of structural joint damage over 5 years of baricitinib treatment in patients with rheumatoid arthritis: Results from RA-BEYOND, *The Journal of Rheumatology*



Supplementary Figure 1. Study design of RA-BEYOND from randomization in the 3 originating studies, RA-BEING, RA-BEAM, and RA-BUILD. Data are included up to 5 years of study treatment and correspond to 240 weeks for RA-BUILD and 244 weeks for RA-BEGIN and RA-BEAM. Patients receiving blinded Bari at the conclusion of phase 3 trials remained on that dose (2 mg or 4 mg QD) in RA-BEYOND. At 52 weeks, DMARD-naïve patients receiving MTX or combination therapy (Bari 4mg + MTX) were switched to Bari 4mg monotherapy; Patients with MTX-IR receiving ADA were switched to Bari 4 mg on background MTX. At 24 weeks, patients with csDMARD-IR receiving PBO were switched to Bari 4 mg on background csDMARD. ADA: adalimumab; Bari: baricitinib; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; DMARD: disease-modifying

antirheumatic drug; IR: inadequate response; MTX: methotrexate; N: number of patients randomized and treated; PBO: placebo; QD: once daily; RA: rheumatoid arthritis. Figure is modified from previously published study design diagram (license: https://creativecommons.org/licenses/by-nc/4.0/legalcode)(1).

Supplementary Table 1. Treatment regimens

Originating Study	Treatment at End of Originating Study	Treatment at Start of RA-BEYOND
RA-BEGIN DMARD-naïve	MTX weekly	Bari 4 mg QD
	Bari 4 mg QD	Bari 4 mg QD
	Bari 4 mg QD + MTX	Bari 4 mg QD
RA-BEAM[a] MTX-IR	PBO QD→Bari 4 mg QD[b] + MTX	Bari 4 mg QD +MTX
	ADA 40 mg SC biweekly +MTX	Bari 4 mg QD +MTX
RA-BUILD[c] csDMARD-IR	PBO QD	Bari 4 mg QD +csDMARD
	Bari 2 mg QD	Bari 2 mg QD +csDMARD
	Bari 4 mg QD	Bari 4 mg QD +csDMARD

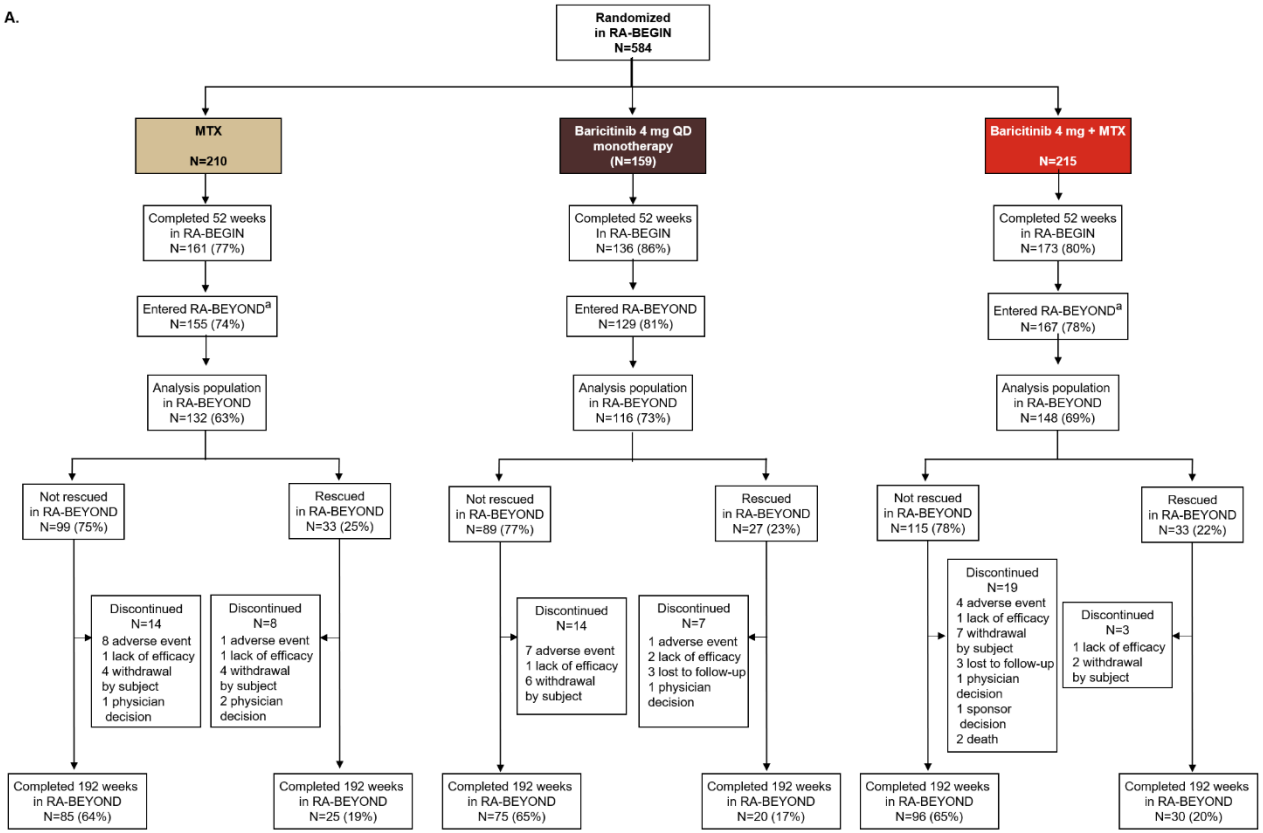
[a]Patients in RA-BEAM were administered treatment with background MTX and could continue receiving background MTX throughout RA-BEYOND.

[b]Patients initially randomized to PBO in RA-BEAM and not rescued were switched to Bari 4 mg QD at week 24.

[c]Patients in RA-BUILD were administered treatment with background csDMARDs and could continue receiving background csDMARDs throughout RA-BEYOND.

ADA: adalimumab; Bari: baricitinib; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; DMARD: disease-modifying antirheumatic drugs; IR: inadequate response; MTX: methotrexate, PBO: placebo; QD: once daily; RA: rheumatoid arthritis; SC: subcutaneous.

A.



Supplementary Table 2. Radiographic assessments during campaigns in the originating phase 3 studies and RA-BEYOND[a]

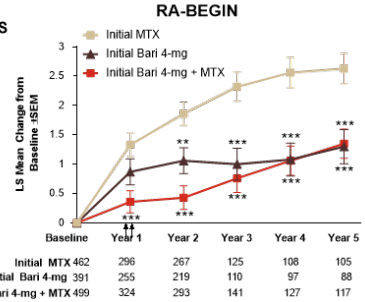
Study	**Campaign**	**Baseline**	**Week 12**	**Week 24**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
RA-BEGIN	1 (RCT)	X	X	X	X				
	2 (year 2)	X			X	X			
	3 (year 5)	X				X	X	X	X
Study	**Campaign**	**Baseline**	**Week 16/20**	**Week 24**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
RA-BEAM	1 (RCT)	X	X	X	X				
	2 (year 2)	X			X	X			
	3 (year 5)	X				X	X	X	X
Study	**Campaign**	**Baseline**	**Week 16/20**	**Week 24**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
RA-BUILD	1 (RCT)	X	X	X					
	2 (year 1)	X	X	X	X				
	3 (year 2)	X			X	X			
	4 (year 5)	X				X	X	X	X

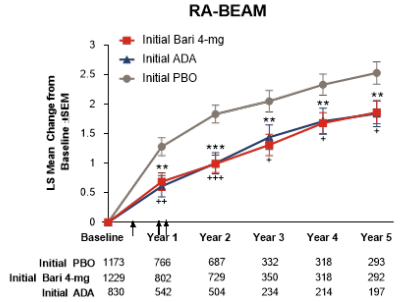
[a]X indicates films that were read or re-read

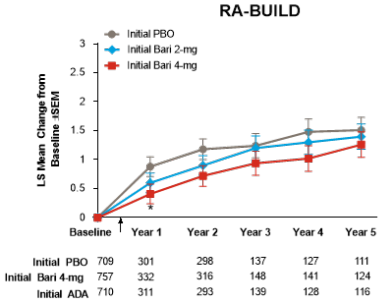
[b]This time point was only in patients who were rescued or discontinued

RA: rheumatoid arthritis; RCT: randomized controlled trial.

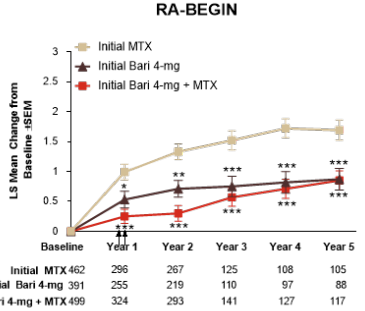
A. mTSS

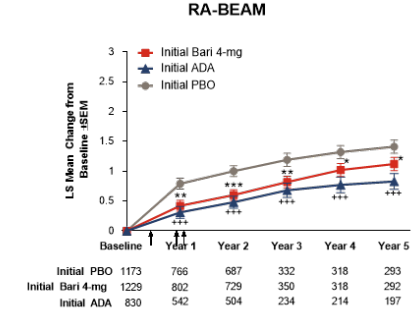


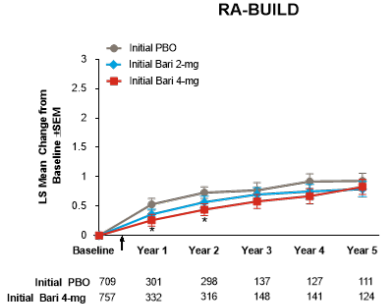




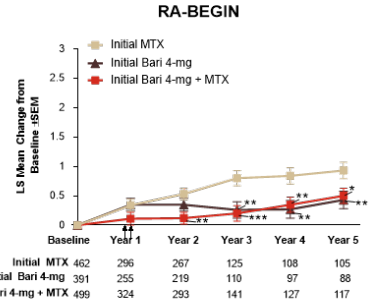
B. ES

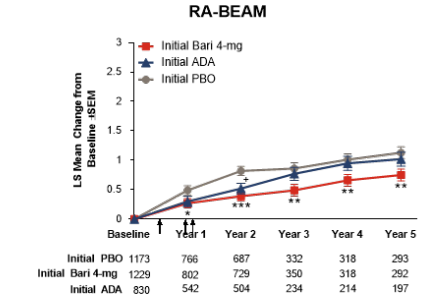


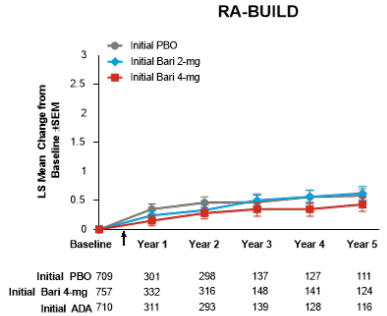




C. JSN

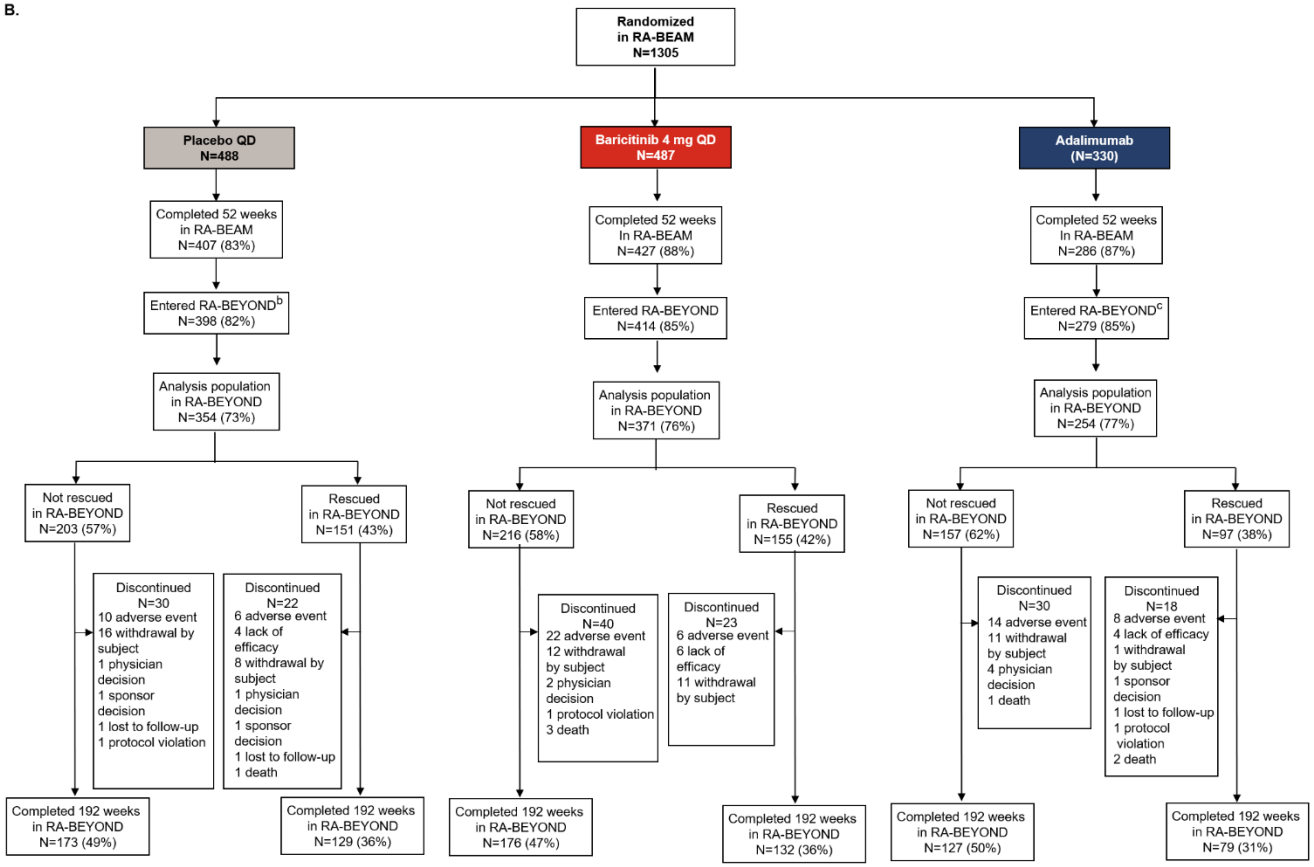




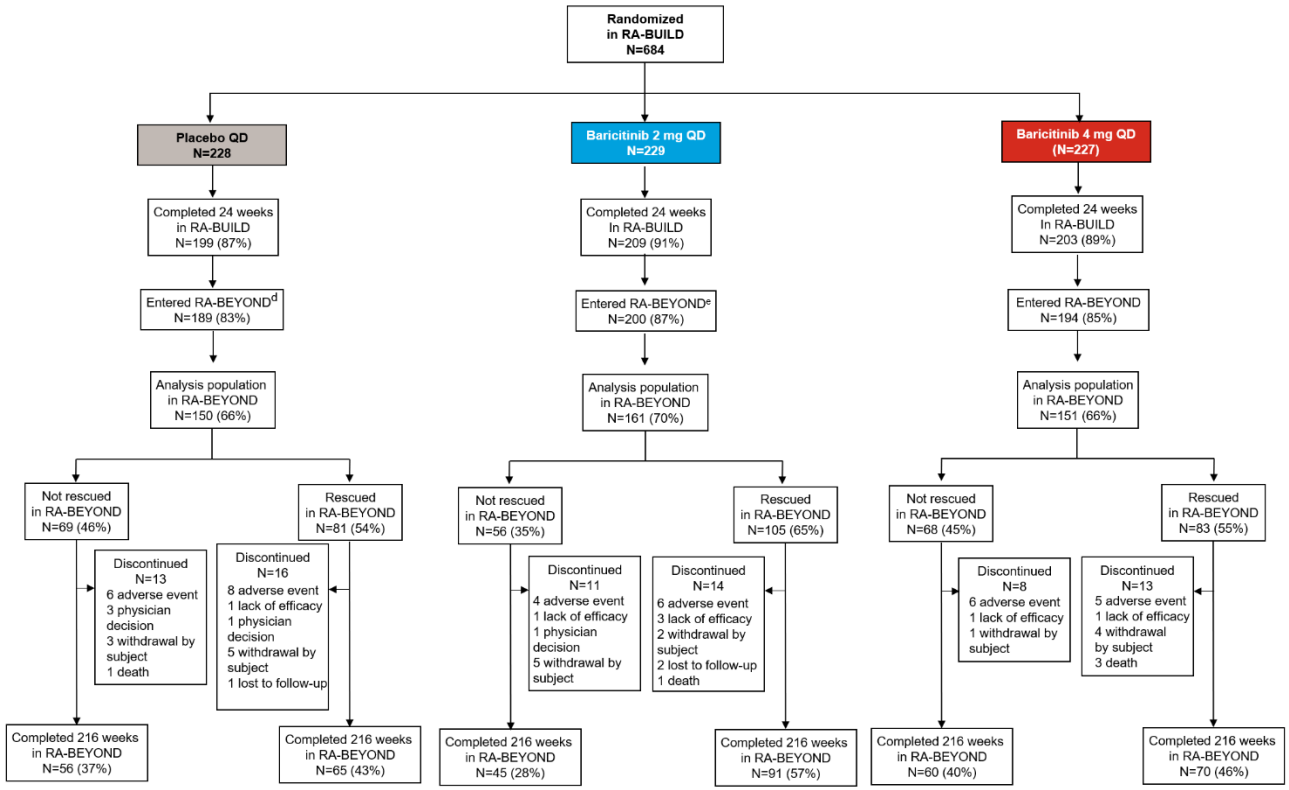


Supplementary Figure 2. Integrated assessment of radiographic progression of structural joint damage by original randomization: Years 1, 2, 3, 4, and 5. The least-squares (LS) mean change from baseline (±standard error of the mean [SEM]) in structural joint damage over time from randomization in the original studies was evaluated using (A) modified Total Sharp Score (mTSS), (B) erosion score (ES), and (C) joint space narrowing (JSN) for patients originally randomized in RA-BEGIN, RA-BEAM or RA-BUILD. The treatment groups indicated are based on original study randomization ('initial' = initial randomized treatment group). The single arrow (PBO) and double arrows (MTX and ADA) on the x axis represent patients on PBO, MTX, or ADA in originating studies switched to Bari 4 mg at 24 or 52 weeks, respectively. Comparisons were analyzed using MMRM with time points nested in different read campaigns. Integrated scores are from the analysis of all patients with radiographic data. Tables below graphs indicate the number of data points available across different read campaigns. *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$ baricitinib 4 mg vs. initial PBO (RA-BEAM; RA-BUILD) or MTX (RA-BEGIN) and baricitinib 4 mg + MTX vs PBO (RA-BEGIN); $^{+}p \leq 0.05$, $^{++}p \leq 0.01$, $^{+++}p \leq 0.001$ ADA vs. PBO (RA-BEAM). ADA: adalimumab; Bari: baricitinib; ES: erosion score; JSN: joint space narrowing; LS: least squares; mTSS: modified Total Sharp Score; MTX: methotrexate; PBO: placebo; RA: rheumatoid arthritis; SEM: standard error of the mean.

B.



c.



Supplementary Figure 3. Patient disposition after 5 years of treatment. Summary of patient disposition in the analysis population of RA-BEYOND (had radiographic assessments at baseline of originating study and at least one radiograph from RA-BEYOND after the 2-year radiograph) originally completing (A) RA-BEGIN, (B) RA-BEAM, or (C) RA-BUILD. Patients from RA-BEGIN and RA-BEAM completed

52 weeks in the originating study and 192 weeks in RA-BEYOND; patients from RA-BUILD completed 24 weeks in the originating study and 216 weeks in RA-BEYOND.

[a]Patients receiving methotrexate or combination therapy in RA-BEGIN were switched to baricitinib 4 mg monotherapy upon entry to RA-BEYOND.

[b]Patients receiving placebo in RA-BEAM were switched to baricitinib 4 mg at week 24.

[c]Patients receiving adalimumab in RA-BEAM were switched to baricitinib 4 mg (plus background csDMARD) upon entry to RA-BEYOND.

[d]Patients receiving placebo in RA-BUILD were switched to baricitinib 4 mg (plus background csDMARDs) upon entry to RA-BEYOND. [e]A total of 200 patients from the baricitinib 2 mg group entered RA-BEYOND from the RA-BUILD study; however, 20 of those patients were rescued to baricitinib 4 mg during the RA-BUILD study, so they entered RA-BEYOND on the 4-mg dose.

csDMARD: conventional synthetic disease-modifying antirheumatic drug; MTX: methotrexate; N: number of patients in specified group; QD: once daily; RA: rheumatoid arthritis.

Supplementary Table 3. Patients who achieved Simplified Disease Activity Index ≤11, nonresponder imputation

	Year 2 (100 weeks)			Year 3 (148 weeks)			Year 4 (196 weeks)			Year 5 (244 weeks)		
	Initial MTX → Bari 4 mg mono	Initial Bari 4 mg	Initial Bari 4 mg + MTX → Bari 4 mg mono	Initial MTX → Bari 4 mg mono	Initial Bari 4 mg	Initial Bari 4 mg + MTX → Bari 4 mg mono	Initial MTX → Bari 4 mg mono	Initial Bari 4 mg	Initial Bari 4 mg + MTX → Bari 4 mg mono	Initial MTX → Bari 4 mg mono	Initial Bari 4 mg	Initial Bari 4 mg + MTX → Bari 4 mg mono
	N=132	N=116	N=148	N=132	N=116	N=148	N=132	N=116	N=148	N=132	N=116	N=148
RA-BEGIN DMARD-naïve Parameter												
SDAI ≤11, n (%)	107 (81.1)	95 (81.9)	121 (81.8)	98 (74.2)	96 (82.8)	124 (83.8)	101 (76.5)	90 (77.6)	111 (75.0)	101 (76.5)	84 (72.4)	105 (71.0)

	Year 2 (100 weeks)			Year 3 (148 weeks)			Year 4 (196 weeks)			Year 5 (244 weeks)		
	Initial PBO → Bari 4 mg	Initial Bari 4 mg	Initial ADA → Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 4 mg	Initial ADA → Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 4 mg	Initial ADA → Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 4 mg	Initial ADA → Bari 4 mg
	N=354	N=371	N=254	N=354	N=371	N=254	N=354	N=371	N=254	N=354	N=371	N=254
RA-BEAM MTX-IR[a] Parameter												
SDAI ≤11, n (%)	277 (78.3)	298 (80.3)	188 (74.0)	276 (78.0)	285 (76.8)	200 (78.7)	270 (76.3)	259 (69.8)	173 (68.1)	250 (70.6)	246 (66.3)	173 (68.1)

	Year 2 (96 weeks)			Year 3 (144 weeks)			Year 4 (192 weeks)			Year 5 (240 weeks)		
	Initial PBO → Bari 4 mg	Initial Bari 2 mg[b]	Initial Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 2 mg[b]	Initial Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 2 mg[b]	Initial Bari 4 mg	Initial PBO → Bari 4 mg	Initial Bari 2 mg[b]	Initial Bari 4 mg
	N=150	N=161	N=151	N=150	N=161	N=151	N=150	N=161	N=151	N=150	N=161	N=151
RA-BUILD csDMARD-IR Parameter												
SDAI ≤11, n (%)	113 (75.3)	109 (67.7)	108 (71.5)	105 (70.0)	110 (68.3)	110 (72.9)	94 (62.7)	105 (65.2)	92 (60.9)	87 (58.0)	94 (58.4)	105 (69.5)

Time points and treatment groups are based on randomization in originating study.

Black arrows indicate patients switched to baricitinib 4 mg at rescue, switch per protocol, or at entry to RA-BEYOND (week 24, initial placebo; week 52 initial MTX, initial MTX + baricitinib 4 mg, initial ADA). Data collected after patients stepped down to Bari 2 mg were imputed using the response rates of the patients who qualified for step-down but were randomized to remain on Bari 4 mg.

[a]Patients in originating study were on background MTX treatment at baseline and throughout the duration of the study

[b]Patients switched to baricitinib 4 mg at rescue.

ADA: adalimumab; Bari: baricitinib; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMARDs: disease-modifying antirheumatic drug; IR: inadequate response; mono: monotherapy; MTX: methotrexate; N: number of patients with baseline and ≥1 radiographic assessment after 2 years and who had data available at the analysis time point; NRI: nonresponder imputation; PBO: placebo; RA: rheumatoid arthritis; SDAI: Simplified Disease Activity Index.

Supplementary Table 4. Patients who achieved Simplified Disease Activity Index ≤11, observed

	Year 2 (100 weeks)			Year 3 (148 weeks)			Year 4 (196 weeks)			Year 5 (244 weeks)		
	Initial MTX → Bari 4 mg mono N-obs=131	Initial Bari 4 mg N-obs=114	Initial Bari 4 mg + MTX → Bari 4 mg mono N-obs=146	Initial MTX → Bari 4 mg mono N-obs=124	Initial Bari 4 mg N-obs=111	Initial Bari 4 mg + MTX → Bari 4 mg mono N-obs=143	Initial MTX → Bari 4 mg mono N-obs=111	Initial Bari 4 mg N-obs=104	Initial Bari 4 mg + MTX → Bari 4 mg mono N-obs=129	Initial MTX → Bari 4 mg mono N-obs=108	Initial Bari 4 mg N-obs=92	Initial Bari 4 mg + MTX → Bari 4 mg mono N-obs=122
RA-BEGIN DMARD-naïve Parameter												
SDAI ≤11, n (%)	107 (81.7)	95 (83.3)	121 (82.9)	98 (79.0)	96 (86.5)	124 (86.7)	101 (91.0)	90 (86.5)	111 (86.1)	101 (93.5)	84 (91.3)	105 (86.1)

	Year 2 (100 weeks)			Year 3 (148 weeks)			Year 4 (196 weeks)			Year 5 (244 weeks)		
	Initial PBO → Bari 4 mg N-obs=351	Initial Bari 4 mg N-obs=368	Initial ADA → Bari 4 mg N-obs=252	Initial PBO → Bari 4 mg N-obs=345	Initial Bari 4 mg N-obs=352	Initial ADA → Bari 4 mg N-obs=238	Initial PBO → Bari 4 mg N-obs=326	Initial Bari 4 mg N-obs=322	Initial ADA → Bari 4 mg N-obs=219	Initial PBO → Bari 4 mg N-obs=302	Initial Bari 4 mg N-obs=302	Initial ADA → Bari 4 mg N-obs=205
RA-BEAM MTX-IR[a] Parameter												
SDAI ≤11, n (%)	277 (78.9)	298 (81.0)	188 (74.6)	276 (80.0)	285 (81.0)	200 (84.0)	270 (82.8)	259 (80.4)	173 (79.0)	250 (82.8)	246 (81.5)	173 (84.4)

	Year 2 (96 weeks)			Year 3 (144 weeks)			Year 4 (192 weeks)			Year 5 (240 weeks)		
	Initial PBO → Bari 4 mg N-obs=148	Initial Bari 2 mg[b] N-obs=157	Initial Bari 4 mg N-obs=150	Initial PBO → Bari 4 mg N-obs=144	Initial Bari 2 mg[b] N-obs=156	Initial Bari 4 mg N-obs=145	Initial PBO → Bari 4 mg N-obs=137	Initial Bari 2 mg[b] N-obs=143	Initial Bari 4 mg N-obs=133	Initial PBO→ Bari 4 mg N-obs=124	Initial Bari 2 mg[b] N-obs=133	Initial Bari 4 mg N-obs=125
RA-BUILD csDMARD-IR Parameter												
SDAI ≤11, n (%)	113 (76.4)	109 (69.4)	108 (72.0)	105 (72.9)	110 (70.5)	110 (75.9)	94 (68.6)	105 (73.4)	92 (69.2)	87 (70.2)	94 (70.7)	105 (84.0)

Black arrows indicate patients switched to baricitinib 4 mg at rescue, switch per protocol, or at entry to RA-BEYOND (week 24, initial placebo; week 52 initial MTX, initial MTX + baricitinib 4 mg, initial ADA). Time points and treatment groups are based on randomization in originating study.

[a]Patients in originating study were on background MTX treatment at baseline and throughout the duration of the study

[b]Patients switched to baricitinib 4 mg at rescue.

ADA: adalimumab; Bari: baricitinib; csDMARD: conventional synthetic DMARD; DMARD: disease-modifying antirheumatic drug; IR: inadequate response; mono: monotherapy; MTX: methotrexate; N-obs: number of patients with baseline and ≥1 radiographic assessment after 2 years and who had data available at the analysis time point; PBO: placebo; RA: rheumatoid arthritis; SDAI: Simplified Disease Activity Index.

Reference

1. van der Heijde D, Schiff M, Tanaka Y, Xie L, Meszaros G, Ishii T, et al. Low rates of radiographic progression of structural joint damage over 2 years of baricitinib treatment in patients with rheumatoid arthritis. RMD Open 2019;5:e000898.