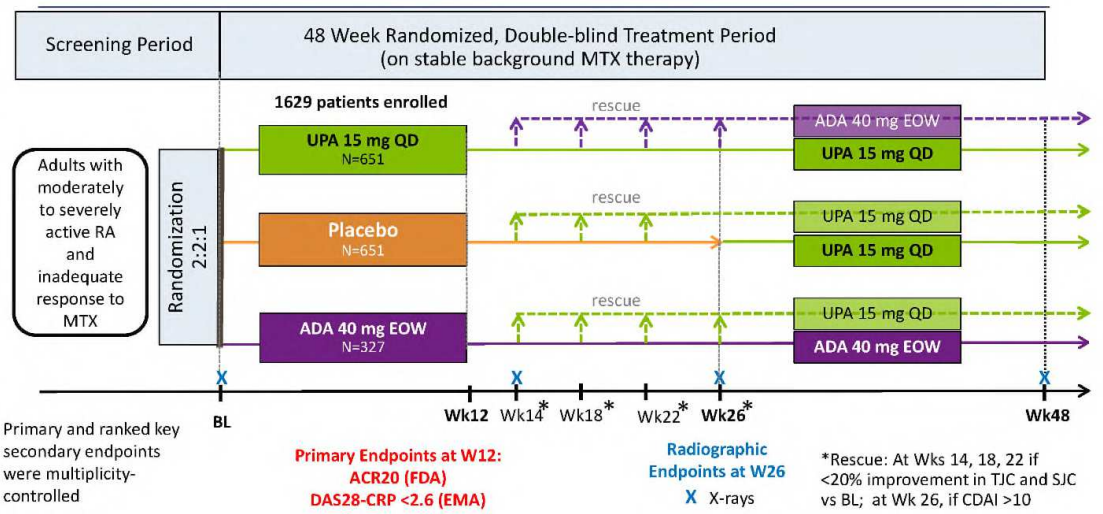
SUPPLEMENTARY MATERIAL

Supplemental Figure 1. Study Design of SELECT-COMPARE



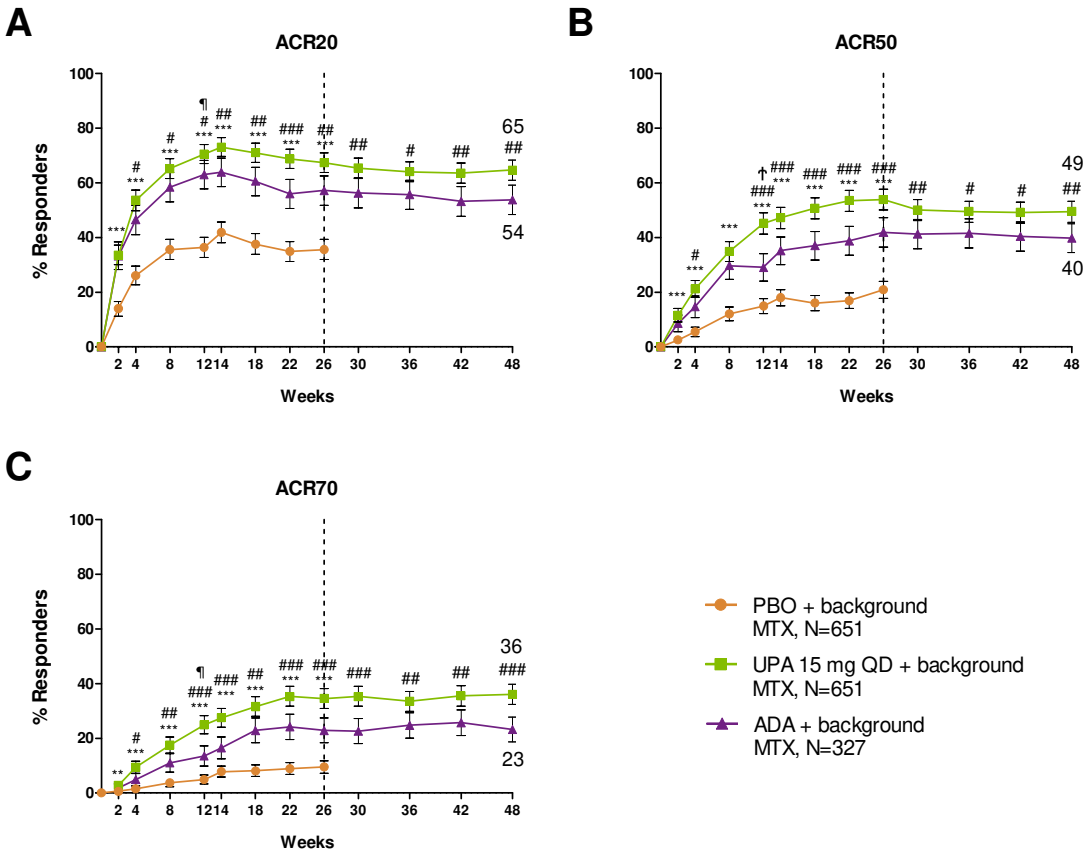
Patients with limited exposure to a bDMARD (<3 months), or patients who had to discontinue a bDMARD due to intolerability (regardless of treatment duration) were allowed to enroll. 9.3% had prior bDMARD exposure.

Supplemental Figure 2. Proportions of patients achieving ACR20, ACR50, and ACR70 responses over 48 weeks (NRI).

Treatment groups are by initial randomisation. Vertical line at Week 26 indicates the end of the placebo-controlled period.
*, p ≤0.05; **, p ≤0.01; ***, p ≤0.001 for comparison of upadacitinib versus placebo; #, p ≤0.05; ##, p ≤0.01; ###, p ≤0.001 for comparison of upadacitinib versus adalimumab.

† Indicates multiplicity-controlled comparisons of upadacitinib vs adalimumab; ¶ Indicates multiplicity-controlled comparisons of upadacitinib vs placebo.

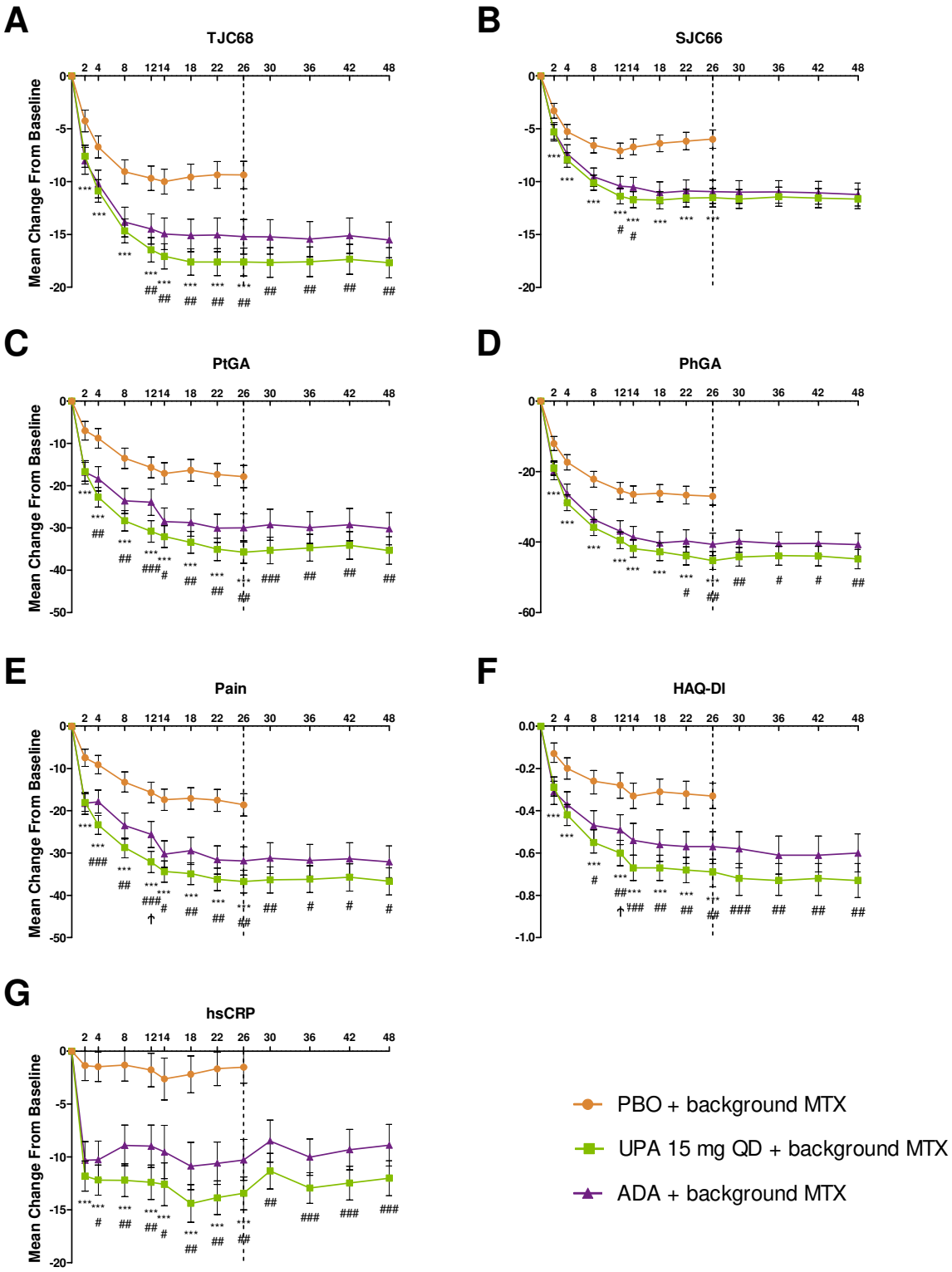
Observations after rescue were handled using NRI (rescue at Weeks 14-22) and LOCF (rescue at Week 26).
ACR, American College of Rheumatology; ACR20/ACR50, 20%/50%/ improvement in ACR score.



Supplemental Figure 3. Least square mean change from Baseline over time in core components of the ACR criteria.

Treatment groups are by initial randomisation. Vertical line at Week 26 indicates the end of the placebo-controlled period.
ANCOVA with LOCF for rescue treatment switch.
*, p ≤0·05; **, p ≤0·01; ***, p ≤0·001 for upadacitinib versus placebo. #, p ≤0·05; ##, p ≤0·01; ###, p ≤0·001 for upadacitinib versus adalimumab.
† Indicates that comparisons between upadacitinib and adalimumab were multiplicity-controlled.

TJC, tender joint count; SJC, swollen joint count; PtGA, patient's global assessment of disease activity; PhGA, Physician's global assessment of disease activity; HAQ-DI, health assessment questionnaire disability index; hsCRP, high-sensitivity C-reactive protein; LOCF, last observation carried forward; ANCOVA, analysis of covariance.

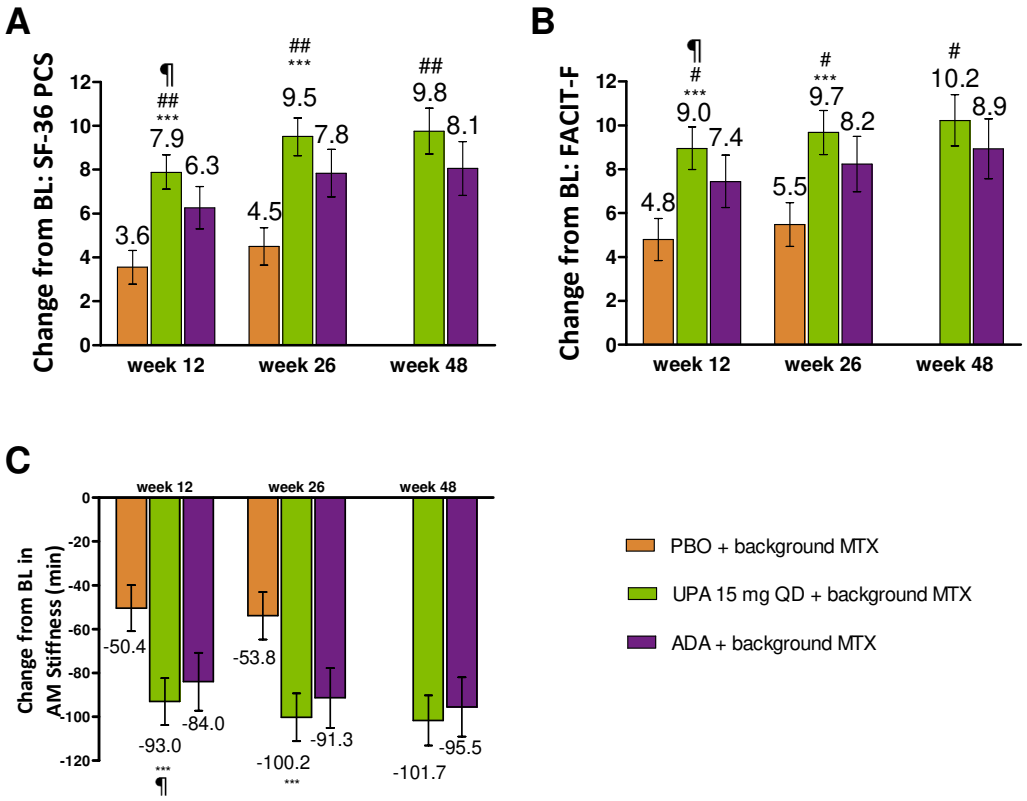

A
TJC68
B
SJC66
C
PtGA
D
PhGA
E
Pain
F
HAQ-DI
G
hsCRP
Mean Change From Baseline
PBO + background MTX
UPA 15 mg QD + background MTX
ADA + background MTX

Supplemental Figure 4. Mean change from Baseline in (A) SF-36 PCS (B) FACIT-F (C) Duration of Morning Stiffness (minutes).

Treatment groups are by initial randomisation.
*, p ≤0·05; **, p ≤0·01; ***, p ≤0·001 for comparison of upadacitinib versus placebo; #, p ≤0·05; ##, p ≤0·01; ###, p ≤0·001 for comparison of upadacitinib versus adalimumab.

Observations after rescue at Week14, 18, 22 or 26 were handled using LOCF.

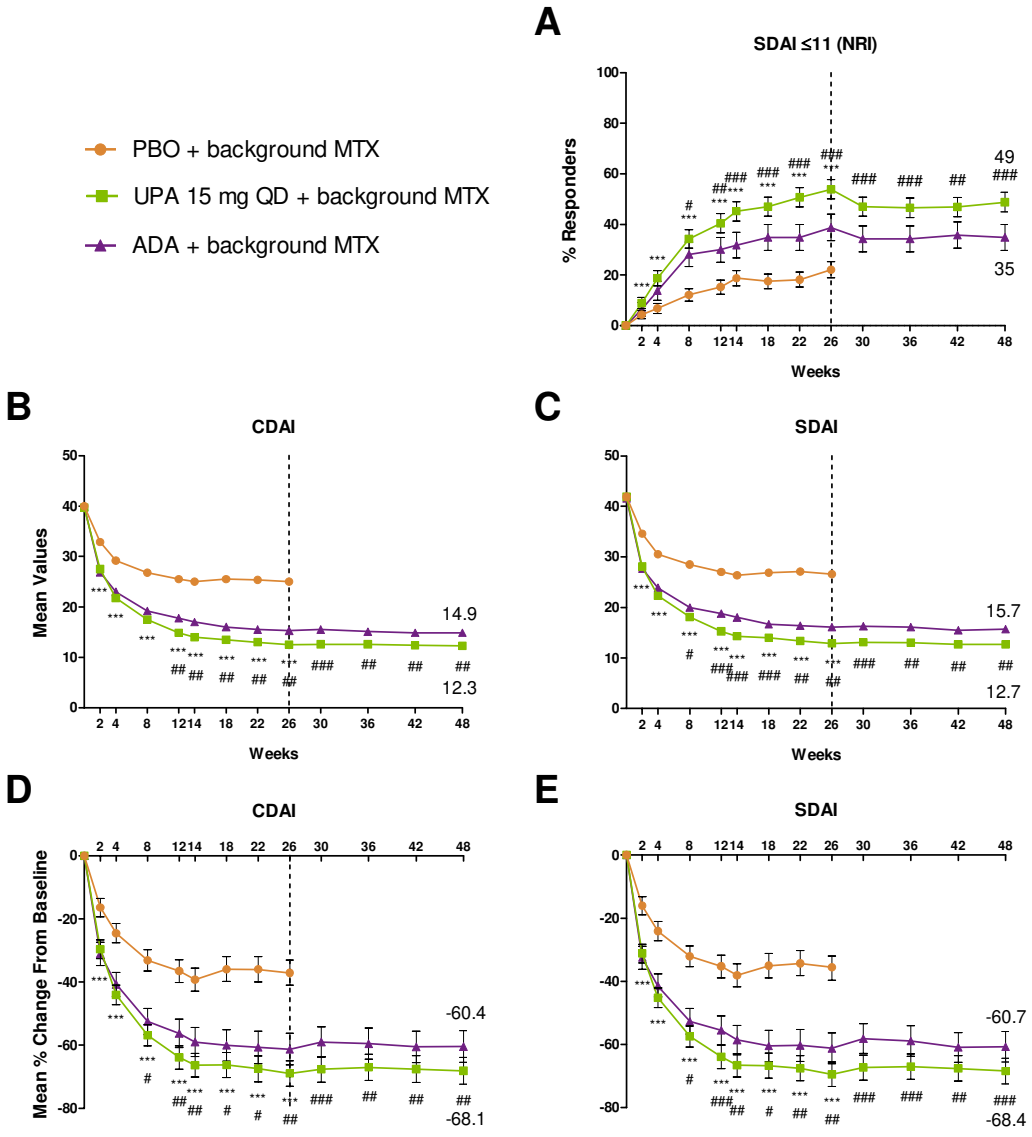
¶ Indicates multiplicity-controlled comparisons of upadacitinib vs placebo.



Supplemental Figure 5. (A) Proportion of patients achieving SDAI ≤11 (NRI) (B-E) Mean and mean percent change from Baseline in CDAI and SDAI (LOCF for rescue treatment).

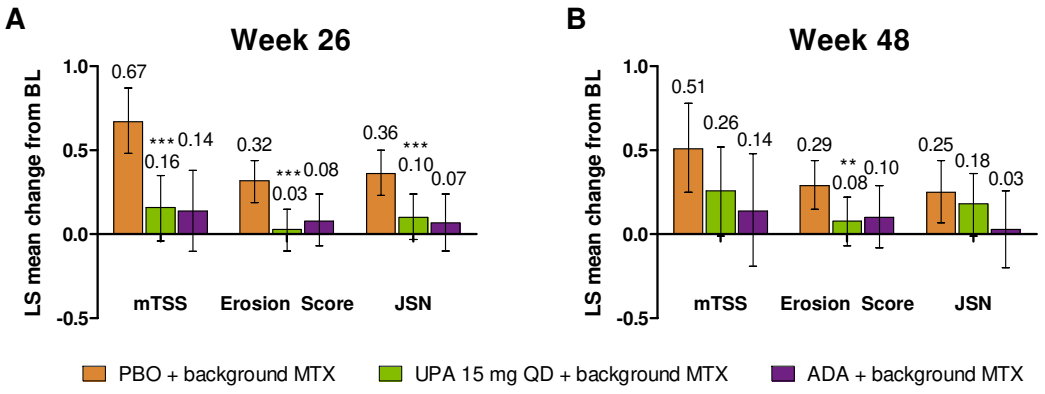
Treatment groups are by initial randomisation. Vertical line at Week 26 indicates the end of the placebo-controlled period.

*, p ≤0·05; **, p ≤0·01; ***, p ≤0·001 for upadacitinib versus placebo. #, p ≤0·05; ##, p ≤0·01; ###, p ≤0·001 for upadacitinib versus adalimumab.

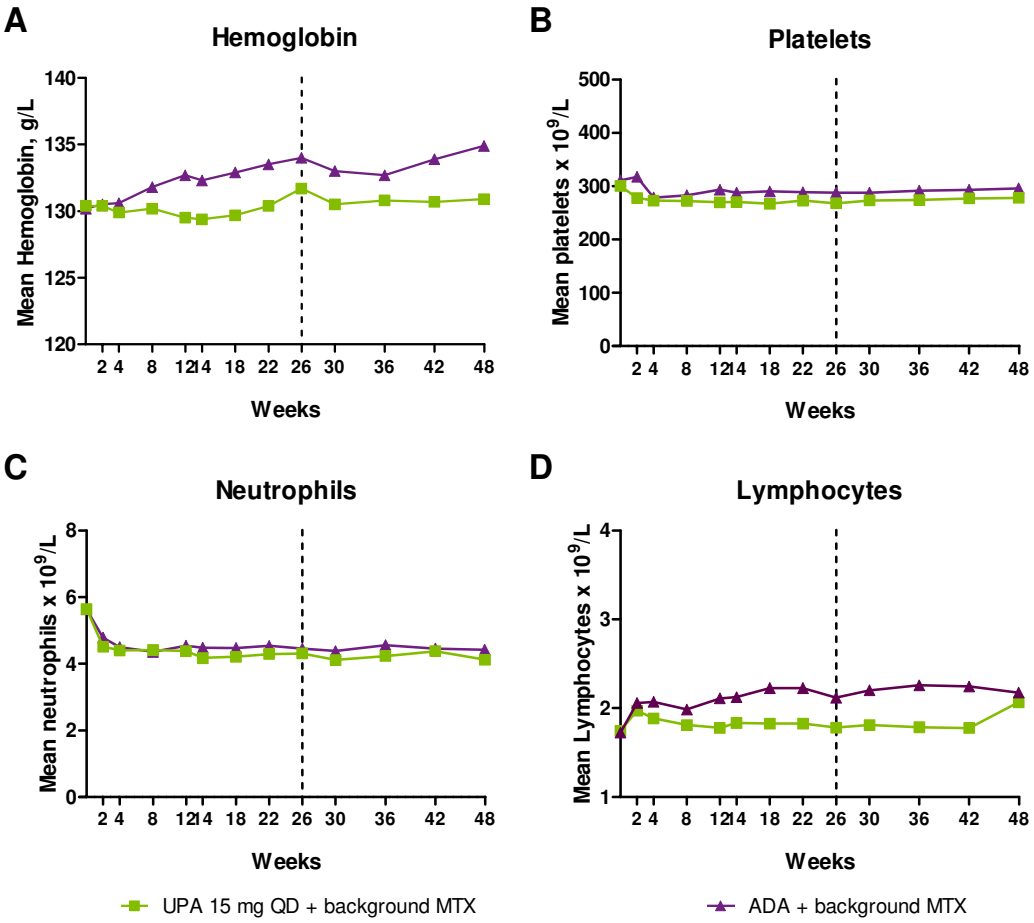


Supplemental Figure 6. Mean change from baseline in mTSS, Erosion and JSN scores at Week 26 and Week 48 (As Observed)

Treatment groups are by initial randomization. Results based on reading session 2.
**, p ≤0.01; ***, p ≤0.001 for comparison of upadacitinib versus placebo.
For radiographic progression, comparisons were not conducted between upadacitinib and adalimumab.

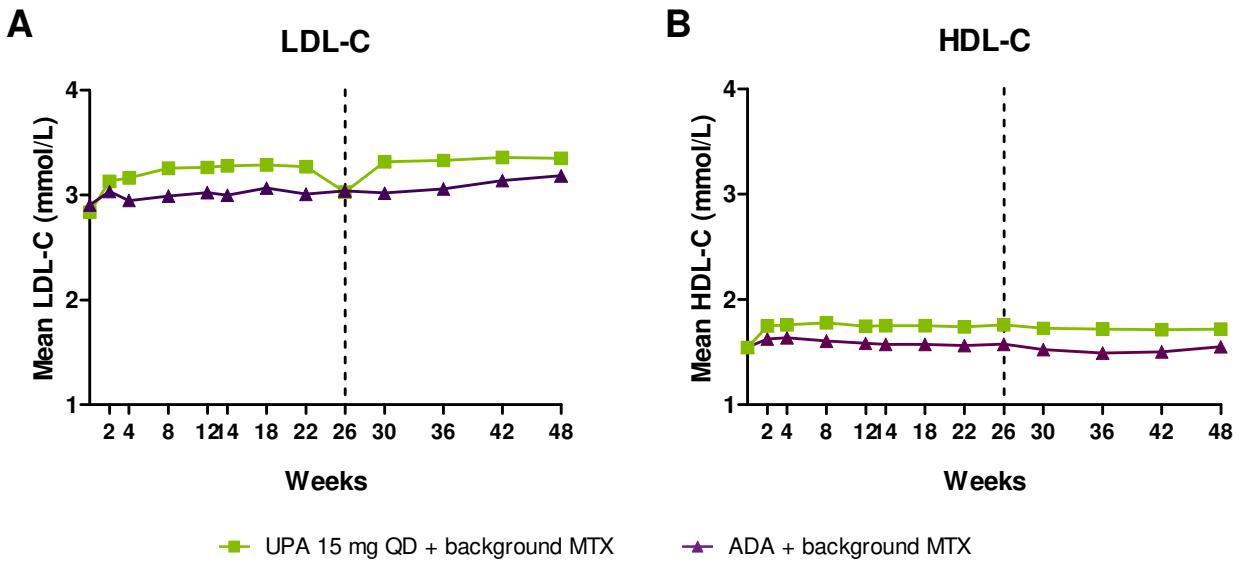


Supplemental Figure 7. Mean values from Baseline to Week 48 in (A) Hemoglobin, (B) Platelets, (C) Neutrophils, and (D) Lymphocytes.



Patients on continuous upadacitinib or adalimumab. Vertical line at Week 26 indicates the end of the placebo-controlled period.

Supplemental Figure 8. Mean values in lipids from Baseline to Week 48.



	Upadacitinib	Adalimumab
LDL-C, mg/dL	19.61 ± 29.22	7.42 ± 25.85
HDL-C, mg/dL	6.3 ± 12.57	1.66 ± 12.17
ALT, U/L	6.1 ± 14.4	1.7 ± 17.7
AST, U/L	6.4 ± 9.8	1.9 ± 12.1

Creatinine, microMol/L	5.6 ± 9.7	2.8 ± 7.4
Creatine Phosphokinase, U/L	78.27 ± 113.43	21.76 ± 55.51
Patients on continuous upadacitinib or adalimumab.		

Supplemental Table 1. Patients with worsening in grade severity (Grade 3 or 4) up to the cut-off date, including single isolated values, n (%)

		Any UPA N=1417, PY=1243.3	**Any ADA N=579, PY=467.8**
Hemoglobin (g/dL)	Grade 3 (decr 2·1 - 2·9 or Hb ≥7·0- <8·0) Grade 4 (decr ≥3·0 or Hb <7·0)	67/1416 (4.7) 19/1416 (1.3)	18/576 (3.1) 6/576 (1.0)
Platelets ($x10^9$/L)	Grade 3 (20 -<50) Grade 4 (<20)	1/1415 (<0.1) 0	0 0
Lymphocytes (x10^9/L)	Grade 3 (0·5 - <1·0) Grade 4 (< 0·5)	250/1416 (17.7) 20/1416 (1.4)	44/576 (7.6) 2/576 (0.3)
Neutrophils (x10^9/L)	Grade 3 (0·5 - <1·0) Grade 4 (< 0·5)	14/1416 (1.0) 4/1416 (0.3)	2/576 (0.3) 1/576 (0.2)
ALT (U/L)	Grade 3 (3·0 - 8·0 x ULN) Grade 4 (> 8·0 x ULN)	47/1414 (3.3) 5/1414 (0.4)	9/577 (1.6) 3/577 (0.5)
AST (U/L)	Grade 3 (3·0 - 8·0 x ULN) Grade 4 (> 8·0 x ULN)	27/1414 (1.9) 3/1414 (0.2)	6/577 (1.0) 4/577 (0.7)
CPK (U/L)	Grade 3 (>5·0 x ULN – 10·0 x ULN) Grade 4 (>10·0 x ULN)	19/1414 (1.3) 4/1414 (0.3)	1/577 (0.2) 1/577 (0.2)
Creatinine (µMoL/L)	Grade 3 (>3·0 - 6·0 x ULN) Grade 4 (>6·0 x ULN)	1/1414 (<0.1) 1/1414 (<0.1)	1/577 (0.2) 0

Grading is based OMERACT criteria, except for CPK and Creatinine, where NCI CTC criteria are used.
†n=646; §n=649; ‡n=651; δn=326

Supplement Table 2. Data Points Plotted in Figure 2

	Weeks											
Parameter (%)	2	4	8	12	14	18	22	26	30	36	42	48
DAS28(CRP) ≤3.2												
PBO	4.6	7.4	11.4	13.8	16.6	15.5	17.8	18.0	N/A	N/A	N/A	N/A
UPA 15 mg QD	14.7	25.5	38.2	45.0	47.5	50.8	53.9	54.7	49.3	49.8	48.5	49.9
ADA 40 mg eow	10.1	17.4	28.4	28.7	30.9	36.1	36.4	38.5	33.9	35.2	35.8	35.2
DAS28(CRP) <2.6												
PBO	2.2	4.0	7.1	6.1	8.8	8.3	9.7	9.2	N/A	N/A	N/A	N/A
UPA 15 mg QD	5.2	13.8	23.5	28.7	32.4	35.6	39.5	40.9	40.4	39.3	39.8	38.2
ADA 40 mg eow	4.3	9.8	16.2	18.0	21.7	26.3	25.7	26.9	22.9	24.2	26.3	27.5
CDAI ≤10												
PBO	4.8	7.2	13.5	16.3	19.8	19.2	20.7	22.1	N/A	N/A	N/A	N/A
UPA 15 mg QD	9.4	18.0	32.7	40.4	45.5	47.9	50.8	52.7	46.2	46.1	46.4	47.3
ADA 40 mg eow	5.8	14.1	27.8	30.0	34.3	35.8	37.0	38.2	35.2	33.9	35.5	34.3
CDAI ≤2.8												
PBO	0.3	0.9	2.3	3.1	3.4	4.8	4.9	5.5	N/A	N/A	N/A	N/A
UPA 15 mg QD	0.6	4.1	9.4	13.4	17.2	16.7	19.0	23.0	23.0	24.1	24.1	25.5
ADA 40 mg eow	0.6	2.1	4.6	7.6	9.2	12.5	13.5	13.8	14.1	15.3	15.9	16.8
SDAI ≤3.3												
PBO	0.3	0.8	1.7	2.8	3.1	3.4	4.5	4.8	N/A	N/A	N/A	N/A
UPA 15 mg QD	0.8	4.1	9.1	12.1	17.5	16.1	19.5	24.3	23.7	23.7	24.4	25.5
ADA 40 mg eow	0.9	2.1	5.2	7.3	9.8	12.5	14.1	13.8	13.1	14.1	15.6	17.4
Boolean Remission												
PBO	0.5	0.9	1.1	2.0	2.6	2.9	3.1	3.8	N/A	N/A	N/A	N/A
UPA 15 mg QD	1.2	3.8	6.8	9.8	14.9	13.8	16.7	18.0	19.5	20.1	20.1	20.9
ADA 40 mg eow	0.3	0.6	2.8	4.0	7.0	9.2	10.1	9.8	10.1	12.5	12.5	14.7

All numbers are %.
DAS28(CRP), 28-joint disease activity score based on C-reactive protein; PBO, placebo; UPA, upadacitinib; QD, once-daily; ADA, adalimumab; eow, every other week; CDAI, clinical disease activity index; SDAI, simplified disease activity index.

Supplement Table 2. Data Points Plotted in Figure 4.

	Weeks											
Parameter (%)	2	4	8	12	14	18	22	26	30	36	42	48
CDAI ≤10												
PBO to UPA	5.0	7.5	14.3	17.6	21.8	26.4	34.1	44.0	56.9	63.7	67.4	67.0
UPA Continued	14.1	27.8	48.6	63.2	69.6	75.1	81.8	93.0	85.1	84.9	86.5	87.8
ADA Continued	11.2	20.9	43.8	52.4	58.9	69.8	71.9	89.1	83.7	81.3	84.8	84.7
UPA to ADA	2.9	3.7	11.3	13.8	17.2	17.3	20.8	14.5	33.5	34.9	38.2	44.5
ADA to UPA	0.7	7.8	14.1	14.0	18.3	21.3	28.6	20.1	45.8	42.8	49.7	57.3
CDAI ≤2.8												
PBO to UPA	0.3	0.9	2.4	3.3	3.7	6.0	9.0	11.8	19.0	21.7	26.2	27.9
UPA Continued	1.0	7.0	15.1	23.7	29.8	29.6	33.9	41.8	43.3	45.6	45.9	48.7
ADA Continued	1.2	3.7	7.5	16.3	17.8	25.2	30.9	32.8	34.1	37.3	39.4	42.0
UPA to ADA	0	0	1.2	0	1.2	0.8	1.2	1.6	3.8	3.4	3.9	5.7
ADA to UPA	0	0.6	1.9	0.6	2.6	4.5	3.4	3.9	7.8	12.4	17.5	18.2
DAS28(CRP) ≤3.2												
PBO to UPA	5.0	7.9	11.7	15.5	18.6	23.7	36.9	41.4	59.1	63.9	69.5	69.6
UPA Continued	22.6	38.9	54.5	70.7	73.0	78.4	86.6	91.1	85.6	85.8	86.1	86.4
ADA Continued	18.5	26.4	45.0	52.1	54.7	71.1	74.1	86.0	78.6	82.3	82.4	80.6
UPA to ADA	4.3	8.0	15.6	18.9	20.4	25.6	29.8	21.4	36.9	33.8	36.6	39.6
ADA to UPA	2.6	10.1	13.9	12.4	17.8	25.3	34.4	28.7	51.7	54.2	56.2	58.6
DAS28(CRP) <2.6												
PBO to UPA	2.3	4.3	7.3	6.7	9.6	12.5	20.2	24.0	39.8	45.9	53.1	52.8
UPA Continued	7.6	22.2	36.3	47.6	52.9	59.6	67.1	72.2	74.9	72.5	75.4	70.8
ADA Continued	8.9	17.0	28.1	34.0	41.0	54.1	54.8	62.5	55.7	59.2	64.1	67.2
UPA to ADA	2.1	2.5	4.8	8.2	9.4	10.5	13.5	8.1	14.2	16.0	18.1	20.4
ADA to UPA	0	3.4	5.7	6.5	9.9	14.7	18.5	14.6	31.1	28.5	39.7	36.6

All numbers are %.
CDAI, clinical disease activity index; DAS28(CRP), 28-joint disease activity score based on C-reactive protein; PBO, placebo; UPA, upadacitinib; ADA, adalimumab.

Malignancies excl. non-melanoma skin cancer included:
In the upadacitinib group, 1 laryngeal cancer, 1 endometrial adenocarcinoma, 1 malignant melanoma, 1 adenocarcinoma gastric, and 1 adenocarcinoma of the colon were reported. Among patients receiving adalimumab, 1 malignant melanoma, 1 colon cancer metastatic), and 1 lung neoplasm malignant were reported.

MACE (including CV death, non-fatal myocardial infarction [MI], non-fatal stroke) included:
Among patients receiving upadacitinib, there was 1 non-fatal stroke, 3 non-fatal MI, and 1 CV death. In the adalimumab group, there was 1 non-fatal stroke and 1 CV death.

Deaths, including non-treatment-emergent (NTE) deaths:
In the upadacitinib group, there were 2 deaths due to undetermined/unknown cause, 1 due to cardiac failure, 1 sudden death, and 1 due to arteriosclerosis coronary artery. Among patients receiving adalimumab, there was 1 death due to left ventricular failure, 1 due to craniocerebral injury, 1 due to colon cancer, and 1 due to mixed connective tissue disease (NTE).

Tuberculosis Testing at Screening:
At screening, all subjects were assessed for evidence of increased risk for TB by a risk assessment form and tested for TB infection by QuantiFERON-TB Gold test. The PPD Skin Test was to be utilized only when a QuantiFERON-TB Gold Test was not possible for any reason (unless both tests were required per local guidelines).
If a subject had a negative PPD test within 90 days prior to Screening and a QuantiFERON-TB Gold test could not be performed by Central Lab at Screening and source documentation was available, TB testing by PPD Skin Test did not need to be repeated, provided nothing had changed in the subject's medical history to warrant a repeat test.
These cases could have been discussed with the AbbVie TA MD. The results of the TB test(s) were to be retained at the site as the original source documentation.
Subjects with a negative TB test and chest x-ray (CXR) not suggestive of active TB or prior TB exposure could have been enrolled.
Subjects with a positive TB test had to be assessed for evidence of active TB versus latent TB, including signs and symptoms and CXR. Subjects with no signs or symptoms and a CXR not suggestive of active TB could have been enrolled after initiation of TB prophylaxis (see below). Subjects with evidence of active TB must not have been enrolled.

Annual TB Screening
For subjects with a negative TB test result at Screening or the most recent evaluation, an annual TB follow-up test was performed. If an annual TB test was newly positive (seroconversion), a chest x-ray (CXR) needed to be performed as soon as possible to aid in distinguishing active versus latent TB. Any positive TB screen after the patient had started the study, should have been reported as an AE of latent TB or active TB (as applicable).
If the subject was experiencing signs or symptoms suspicious for TB or something had changed in the subject's medical history to warrant a repeat test before the next scheduled annual TB re-test, the case (including the TB test results) had to be discussed with the AbbVie TA MD.