

Supplementary Materials

Supplementary Table S1 Baseline demographics and clinical characteristics

Characteristics	PBO (n=651)	UPA 15 mg QD (n=651)	ADA 40 mg EOW (n=327)
Female, n (%)	512 (79)	521 (80)	259 (79)
Disease duration, years	8 ± 8	8 ± 8	8 ± 8
Age, years	54 ± 12	54 ± 12	54 ± 12
RF+ and/or ACPA+, n (%)	571 (88)	566 (87)	288 (88)
MTX dose, mg/week	16.8 ± 3.8	17.0 ± 4.2	17.1 ± 3.8
Prior bDMARD exposure, n (%)	63 (10)	54 (8)	34 (10)
Oral GC use, n (%)	392 (60)	388 (60)	202 (62)
Dose, mg*	6.3 ± 2.4	6.2 ± 2.3	6.5 ± 2.4
TJC68	26 ± 14	26 ± 15	26 ± 15
SJC66	16 ± 9	17 ± 10	16 ± 9
PtGA (100-mm VAS)	64 ± 21	64 ± 22	66 ± 21
PhGA (100-mm VAS)	66 ± 18	66 ± 17	65 ± 18
Pain (100-mm VAS)	65 ± 21	66 ± 21	66 ± 21
hsCRP, mg/L	18 ± 22	18 ± 22	20 ± 22
DAS28(CRP) (scale 0–10)	5.8 ± 0.9	5.8 ± 1.0	5.9 ± 1.0
DAS28(ESR) (scale 0–10)	6.5 ± 1.0	6.4 ± 1.0	6.5 ± 1.0
CDAI (scale 0–76)	40 ± 13	40 ± 13	40 ± 13
HAQ-DI (scale 0–3)	1.6 ± 0.6	1.6 ± 0.6	1.6 ± 0.6
mTSS (scale 0–448)	36 ± 52	34 ± 50	35 ± 47
Erosion score (scale 0–168)	17 ± 27	17 ± 26	15 ± 23
JSN score (scale 0–280)	19 ± 26	18 ± 25	19 ± 26
Duration of morning stiffness, minutes	142 ± 170	142 ± 188	146 ± 185
FACIT-F score (scale 0–52)	27 ± 11	27 ± 11	26 ± 11
SF-36 PCS score (scale 0–100)	33 ± 7	33 ± 7	32 ± 7

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Data are mean \pm standard deviation unless stated otherwise. *Based on prednisone or equivalent daily dose. ADA, adalimumab; ACPA+, anti-cyclic citrullinated peptide positive; bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score based on C-reactive protein; DAS28(ESR), 28-joint Disease Activity Score using erythrocyte sedimentation rate; EOW, every other week; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; SF-36 PCS, 36-item Short Form physical component summary; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire – Disability Index; hsCRP, high-sensitivity C-reactive protein; JSN, joint space narrowing; MTX, methotrexate; mTSS, modified Total Sharp Score; PBO, placebo; PhGA, physician’s global assessment of disease activity; PtGA, patient’s global assessment of disease activity; QD once daily; RF+, rheumatoid factor positive; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; UPA, upadacitinib, VAS, visual analogue scale.

Supplementary Table S2 Observed COVID-19 infections in patients receiving upadacitinib and adalimumab		
Parameter, n (%)	Any UPA 15 mg QD (n=1417)	Any ADA 40 mg EOW (n=579)
COVID-19 infection	202 (14.3)	59 (10.2)
Serious	52 (25.7)	6 (1.0)
Fatal	10 (5.0)	0
Age at baseline, years		
Mean (SD)	51.0 (11.4)	51.5 (10.2)
Median (min, max)	51.0 (20, 82)	54.0 (21, 70)
Geographical region		
North America	20 (9.9)	9 (15.3)
South/Central America	63 (31.2)	14 (23.7)
Western Europe	7 (3.5)	2 (3.4)
Eastern Europe	94 (46.5)	28 (47.5)
Asia	6 (3.0)	1 (1.7)
Other	12 (5.9)	5 (8.5)
Severity		
Mild	64 (31.7)	18 (30.5)
Moderate	99 (49.0)	37 (62.7)
Severe	39 (19.3)	4 (6.8)
Infection leading to hospitalisation		
Yes	49 (24.3)	6 (10.2)
No	27 (13.4)	5 (8.5)
Missing	126 (62.4)	48 (81.4)
Action taken with study drug		
Dose not changed	50 (24.8)	23 (39.0)
Dose interrupted	136 (67.3)	35 (59.3)
Drug withdrawn	16 (7.9)	1 (1.7)
Multiple (interrupted, withdrawn)	0	0

Safety was assessed up to week 264, through the cut-off date of 5 October 2022. Treatment-emergent adverse events included any adverse event with an onset date on or after the first dose of study drug and up to 30 days after the last dose of placebo or UPA and 70 days for ADA, if patients discontinued prematurely. Data through 264 weeks include all patients receiving UPA or ADA, including rescue groups, with assignment based on drug exposure at the time of the event. ADA, adalimumab; EOW, every other week; QD, once daily; SD, standard deviation; UPA, upadacitinib.

Supplementary Table S3 Most common TEAEs through 264 weeks		
EAER	Any UPA 15 mg QD (n=1417; PY=4496.6) E (E/100 PY)	Any ADA 40 mg EOW (n=579; PY=1472.4) E (E/100 PY)
Urinary tract infection	326 (7.2)	114 (7.7)
Upper respiratory tract infection	276 (6.1)	74 (5.0)
Nasopharyngitis	265 (5.9)	75 (5.1)
Bronchitis	194 (4.3)	71 (4.8)
ALT elevation	193 (4.3)	44 (3.0)
CPK elevation	179 (4.0)	26 (1.8)
Hypertension	168 (3.7)	46 (3.1)
AST elevation	156 (3.5)	29 (2.0)
Worsening of RA	151 (3.4)	82 (5.6)

Safety was assessed up to week 264, through the cut-off date of 5 October 2022. TEAEs included any adverse event with an onset date on or after the first dose of study drug and up to 30 days after the last dose of placebo or UPA and 70 days for ADA, if patients discontinued prematurely. Data through 264 weeks include all patients receiving UPA or ADA, including rescue groups, with assignment based on drug exposure at the time of the event. ADA, adalimumab; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; E, events, EAER, exposure-adjusted event rate; EOW, every other week; PY patient-years, QD, once daily; RA, rheumatoid arthritis; TEAE, treatment-emergent adverse event; UPA, upadacitinib.

Supplementary Table S4 Treatment-emergent: malignancies, adjudicated MACE and adjudicated VTE		
System organ class MedDRA 25.0 preferred term	Any UPA 15 mg QD (n=1417; PY=4496.6) E (E/100 PY) [95% CI]	Any ADA 40 mg EOW (n=579; PY=1472.4) E (E/100 PY) [95% CI]
Malignancies		
Skin		
Basal cell carcinoma	10 (0.2) [0.1, 0.4]	1 (<0.1) [0.0, 0.4]
Bowen's disease	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Carcinoma <i>in situ</i> of the skin	1 (<0.1) [0.0, 0.3]	0 [0.0, 0.1]
Malignant melanoma	3 (<0.1) [0.0, 0.2]	1 (<0.1) [0.0, 0.4]
Neuroendocrine carcinoma of the skin	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Squamous cell carcinoma of the skin	9 (0.2) [0.1, 0.4]	1 (<0.1) [0.0, 0.4]
Gastrointestinal tract		
Adenocarcinoma gastric	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Adenocarcinoma of the colon	1 (<0.1) [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Colon cancer	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Colon cancer metastatic	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Rectal adenocarcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Lung		
Large cell lung cancer	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Lung adenocarcinoma	3 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]
Lung carcinoma cell type unspecified stage IV	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Lung neoplasm malignant	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Lung squamous cell carcinoma stage IV	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Breast		
Breast cancer	2 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]
Breast cancer metastatic	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Intraductal proliferative breast lesion	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Invasive ductal breast carcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Female reproductive system		
Endometrial adenocarcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Ovarian endometrioid carcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Squamous cell carcinoma of the vulva	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Vulval cancer	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Lymphatic system		
B cell lymphoma	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Diffuse large B cell lymphoma	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Hodgkin's disease stage IV	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Bone		
Metastases to bone	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Metastases to bone marrow	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
Oral cavity/larynx		
Squamous cell carcinoma of the oral cavity	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Laryngeal cancer	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Urinary tract		
Bladder transitional cell carcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Brain/eye		
Glioblastoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Other organ systems		

Supplementary Table S4 Treatment-emergent: malignancies, adjudicated MACE and adjudicated VTE		
System organ class MedDRA 25.0 preferred term	Any UPA 15 mg QD (n=1417; PY=4496.6) E (E/100 PY) [95% CI]	Any ADA 40 mg EOW (n=579; PY=1472.4) E (E/100 PY) [95% CI]
Adenocarcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Malignant neoplasm of unknown primary site	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Metastatic squamous cell carcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Myxoid liposarcoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Squamous cell carcinoma	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
MACE* and other CV events		
<i>CV death</i>		
Sudden cardiac death	4 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]
Heart failure	0 [0.0, 0.1]	1 (<0.1) [0.0, 0.4]
PE [†]	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
<i>Non-fatal myocardial infarction</i>	4 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]
<i>Non-fatal stroke</i>	3 (<0.1) [0.0, 0.2]	3 (0.2) [0.0, 0.6]
<i>Undetermined/unknown cause of death</i>	6 (0.1) [0.0, 0.3]	1 (<0.1) [0.0, 0.4]
<i>Other CV events (non-fatal)</i>		
CV procedures	1 (<0.1) [0.0, 0.1]	2 (0.1) [0.0, 0.5]
Unstable angina requiring hospitalisation	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
Hospital-based treatment for heart failure	3 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]
Transient ischaemic attack	4 (<0.1) [0.0, 0.2]	2 (0.1) [0.0, 0.5]
VTE[‡]		
<i>Fatal</i>		
PE	1 (<0.1) [0.0, 0.1]	0 [0.0, 0.3]
<i>Non-fatal</i>		
DVT	7 (0.2) [0.1, 0.3]	2 (0.1) [0.0, 0.5]
PE	7 (0.2) [0.1, 0.3]	4 (0.3) [0.1, 0.7]
DVT and PE (concurrent)	3 (<0.1) [0.0, 0.2]	0 [0.0, 0.3]

Safety was assessed up to week 264, through the cut-off date of 5 October 2022. Treatment-

emergent adverse events included any adverse event with an onset date on or after the first dose of study drug and up to 30 days after the last dose of placebo or UPA and 70 days for ADA, if patients discontinued prematurely. Data through 264 weeks include all patients receiving UPA or ADA, including rescue groups, with assignment based on drug exposure at the time of the event. *MACE defined as CV death (includes acute MI, sudden cardiac death, heart failure, CV procedure-related death, death due to CV haemorrhage, fatal stroke, PE and other CV causes), non-fatal MI and non-fatal stroke. [†]Also included under VTE. [‡]VTE included DVT and PE (fatal and non-fatal). A concurrent DVT and PE event will be counted under both the 'DVT' row and the 'PE' row, as well as under the 'DVT and PE (concurrent)' row. ADA, adalimumab; CI, confidence interval; CV, cardiovascular; DVT,

deep vein thrombosis; E, events; EOW, every other week; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; PE, pulmonary embolism; PY, patient-years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolic event.

Supplementary Table S5 History of patients with MACE			
Treatment group	Type of MACE*	Age at start of study	Relevant medical history
Any UPA	CV death	77	Hypertensive since 2001, former smoker for 56 years
Any UPA	CV death	73	Diabetes mellitus since 2010, hypothyroidism since 2011
Any UPA	CV death [§]	74	Hypertension, obesity (BMI 36.1), trauma, recent immobilisation due to fall, former smoker
Any UPA	CV death	58	Hypertension since 2010, diabetes mellitus since 2014, obesity (BMI 41.8)
Any UPA	CV death	57	Cardiopulmonary arrest, hypertension, former smoker
Any ADA	CV death	66	Pre-existing cardiac condition on ECG (left ventricular hypertrophy), hypertension since 1987, diabetes mellitus since 2014, history of chronic bronchitis, recent event of exacerbation of chronic bronchitis, obesity (BMI 34.0)
Any UPA	Non-fatal MI [†]	68	Hypertensive since 2014, current smoker for 40 years
Any UPA	Non-fatal MI	42	Hypertension, dyslipidaemia, and diabetes mellitus since 2011; former cigarette smoker for 10 years, current cigar smoker, obesity (BMI 58.2)
Any UPA	Non-fatal MI [‡]	53	Pre-existing cardiac condition on ECG (left atrial enlargement), history of diabetes mellitus, obesity (BMI 33.5)
Any UPA	Non-fatal MI	51	Hyperlipidaemia, former smoker for 20 years
Any UPA	Non-fatal stroke	39	Patent foramen ovale, hypercholesterolaemia, current smoker for 20 years
Any UPA	Non-fatal stroke	55	Obesity since 2007 (BMI 42.8), hypertension since 2009, diabetes mellitus since 2015, current smoker for 36 years
Any UPA	Non-fatal stroke	70	History of paroxysmal atrial fibrillation
Any ADA	Non-fatal stroke	57	Hypertension since 2009, current smoker for 41 years, thrombolysis therapy for treatment of TEAE of PE
Any ADA	Non-fatal stroke [‡]	71	Hypertension since 1998, hypercholesterolaemia since 2016
Any ADA	Non-fatal stroke	59	Hypertension since 2004, hyperlipidaemia and diabetes mellitus since 2009, atrial fibrillation since 2015, obesity (BMI 43.9)

Safety was assessed up to week 264, through the cut-off date of 5 October 2022. Treatment-emergent adverse events included any adverse event with an onset date on or after the first dose of study drug and up to 30 days after the last dose of PBO or UPA and 70 days for ADA, if patients discontinued

prematurely. Some patients had more than one event. Data through 264 weeks include all patients receiving UPA or ADA, including rescue groups, with assignment based on drug exposure at the time of the event. Obesity was defined as a BMI ≥ 30.0 . *MACE defined as CV death (includes acute MI, sudden cardiac death, heart failure, CV procedure-related death, death due to CV haemorrhage, fatal stroke, PE and other cardiovascular causes), non-fatal MI and non-fatal stroke. †Patient also had a serious adverse event adjudicated as non-fatal MI during exposure to PBO (study day 70; 114 days prior to treatment switch). ‡Reasonable possibility of being related to study drug per investigator. §Included PE which counted towards both MACE and venous thromboembolic event. ADA, adalimumab; BMI, body mass index; CV, cardiovascular; ECG, electrocardiogram; MACE, major adverse cardiovascular event; MI, myocardial infarction; PBO, placebo; PE, pulmonary embolism; TEAE, treatment-emergent adverse event; UPA, upadacitinib.

Supplementary Table S6 History of patients with VTE

Treatment group	Type of VTE*	Age at start of study	Relevant medical history
Any UPA	PE [†]	44	Hypertension since 2015, oral contraceptive use, recent hospitalisation, obesity (BMI 31.2)
Any UPA	PE [†]	63	Obesity since 1990 (BMI of 37.5), hypertension since 2015, former smoker for 35 years, family history of PE (patient's sister)
Any UPA	PE	63	History of PE, former smoker, congestive heart failure
Any ADA	PE [†]	52	History of hypertension with hypertonic angiopathy, obesity (BMI 32.0), concomitant glucocorticoids, concurrent event of worsening dyspnoea
Any ADA	PE	69	Hypertension since 2000, history of obesity and Takotsubo cardiomyopathy, obesity (BMI 41.3), former smoker for 31 years
Any ADA	PE	57	Hypertension since 2009, current smoker for 41 years
Any ADA	PE	65	Obesity since 1974 (BMI 47.3), diabetes mellitus since 2004, hypertension since 2005, former smoker for 15 years, concomitant use of celecoxib
Any ADA	PE	60	Hypertension since 1984, history of obesity and lung fibrosis, obesity (BMI 64.0), former smoker for 22 years
Any UPA	DVT [†]	51	Dyslipidaemia since 2016, hypertension since 2017, obesity (BMI 35.5), former smoker for 8 years, recent prolonged sitting due to travel for 3 hours
Any UPA	DVT [†]	34	Hormonal contraceptive use, methylprednisolone use, obesity (BMI 39.7)
Any UPA	DVT	47	Hypercholesterolaemia, atrial fibrillation
Any ADA	DVT	67	Hypertension since 2012, obstructive sleep apnoea since 2014, history of PE, cardiac murmur, hyperlipidaemia, obesity (BMI 41.8)
Any ADA	DVT [†]	61	Peripheral vascular venous disease since 1992, hypertension since 2008, sedentary lifestyle
Any ADA	DVT	66	Hypertension, congestive heart failure, lower extremity varicose veins, recent leg muscle strain, former smoker
Any UPA	DVT and PE	51	History of prior DVT, current smoker for 35 years
Any UPA	DVT and PE [†]	36	Oral contraceptive use, recent lower extremity trauma, obesity (BMI 31.2)
Any UPA	CV death [‡]	74	Hypertension, obesity (BMI 36.1), trauma, recent immobilisation due to fall, former smoker

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[†]Reasonable possibility of being related to study drug per investigator. [‡]Included PE which counted towards both major adverse cardiovascular event and VTE. ADA, adalimumab; BMI, body mass index; CV, cardiovascular; DVT, deep vein thrombosis; PE, pulmonary embolism; UPA, upadacitinib; VTE, venous thromboembolic event.

Supplementary Table S7 Treatment-emergent: deaths		
System organ class MedDRA 25.0 preferred term	Any UPA 15 mg QD (n=1417; PY=4496.6) E (E/100 PY)	Any ADA 40 mg EOW (n=579; PY=1472.4) E (E/100 PY)
Deaths		
<i>Cardiac disorders</i>		
Acute myocardial infarction	2 (<0.1)	0
Arteriosclerosis coronary artery	1 (<0.1)	0
Cardiac arrest	1 (<0.1)	0
Cardiac failure	3 (<0.1)	0
Cardiorespiratory arrest	2 (<0.1)	0
Cardiopulmonary failure	0	1 (<0.1)
Hypertensive heart disease	1 (<0.1)	0
Left ventricular failure	0	1 (<0.1)
Myocardial infarction	2 (<0.1)	0
<i>General disorders and administration site conditions</i>		
Death	4 (<0.1)	0
Multiple organ dysfunction syndrome	2 (<0.1)	1 (<0.1)
Sudden death	1 (<0.1)	1 (<0.1)
<i>Infections and infestations</i>		
COVID-19	4 (<0.1)	0
COVID-19 pneumonia	6 (0.1)	0
Meningitis listeria	1 (<0.1)	0
Nosocomial infection	1 (<0.1)	0
Pneumonia	1 (<0.1)	1 (<0.1)
Sepsis	1 (<0.1)	0
<i>Injury, poisoning and procedural complications</i>		
Craniocerebral injury	0	1 (<0.1)
Pelvic fracture	1 (<0.1)	0
<i>Musculoskeletal and connective tissue disorders</i>		
Mixed connective tissue disease	0	1 (<0.1)
<i>Neoplasms benign, malignant and unspecified (including cysts and polyps)</i>		
Colon cancer metastatic	0	1 (<0.1)
Diffuse large B cell lymphoma	0	1 (<0.1)
Lung carcinoma cell type unspecified stage IV	1 (<0.1)	0
Lung squamous cell carcinoma stage IV	0	1 (<0.1)
Malignant neoplasm of unknown primary site	1 (<0.1)	0
<i>Respiratory, thoracic and mediastinal disorders</i>		
Acute respiratory distress syndrome	1 (<0.1)	0
Respiratory failure*	1 (<0.1)	0

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emergent adverse events included any adverse event with an onset date on or after the first dose of study drug and up to 30 days after the last dose of placebo or UPA and 70 days for ADA, if patients

discontinued prematurely. Data through 264 weeks include all patients receiving UPA or ADA, including rescue groups, with assignment based on drug exposure at the time of the event.

*Respiratory failure related to COVID-19. ADA, adalimumab; E, events; EOW, every other week; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years; QD, once daily; UPA, upadacitinib.

Supplementary Table S8 Proportions of patients achieving CDAI LDA (≤ 10)/remission (≤ 2.8), DAS28(CRP) ≤ 3.2 / < 2.6 , ACR20, ACR50 and ACR70 through 264 weeks (NRI)

n/N (%)	Weeks										
	12	26	48	60	72	84	96	108	120	132	144
CDAI ≤ 10											
UPA	263/651 (40.4)	343/651 (52.7)	299/651 (45.9)	299/651 (45.9)	294/651 (45.2)	290/651 (44.5)	285/651 (43.8)	276/651 (42.4)	277/651 (42.5)	271/651 (41.6)	265/651 (40.7)
ADA	98/327 (30.0)	125/327 (38.2)	107/327 (32.7)	107/327 (32.7)	104/327 (31.8)	99/327 (30.3)	98/327 (30.0)	100/327 (30.6)	99/327 (30.3)	102/327 (31.2)	96/327 (29.4)
CDAI ≤ 2.8											
UPA	87/651 (13.4)	150/651 (23.0)	166/651 (25.5)	160/651 (24.6)	183/651 (28.1)	176/651 (27.0)	177/651 (27.2)	163/651 (25.0)	169/651 (26.0)	170/651 (26.1)	159/651 (24.4)
ADA	25/327 (7.6)	45/327 (13.8)	55/327 (16.8)	49/327 (15.0)	54/327 (16.5)	56/327 (17.1)	53/327 (16.2)	53/327 (16.2)	51/327 (15.6)	55/327 (16.8)	60/327 (18.3)
DAS28(CRP) ≤ 3.2											
UPA	293/651 (45.0)	356/651 (54.7)	297/651 (45.6)	286/651 (43.9)	293/651 (45.0)	283/651 (43.5)	282/651 (43.3)	284/651 (43.6)	275/651 (42.2)	269/651 (41.3)	253/651 (38.9)
ADA	94/327 (28.7)	126/327 (38.5)	105/327 (32.1)	99/327 (30.3)	96/327 (29.4)	93/327 (28.4)	93/327 (28.4)	104/327 (31.8)	95/327 (29.1)	95/327 (29.1)	90/327 (27.5)
DAS28(CRP) < 2.6											
UPA	187/651 (28.7)	266/651 (40.9)	243/651 (37.3)	247/651 (37.9)	259/651 (39.8)	256/651 (39.3)	242/651 (37.2)	238/651 (36.6)	242/651 (37.2)	236/651 (36.3)	215/651 (33.0)
ADA	59/327 (18.0)	88/327 (26.9)	87/327 (26.6)	79/327 (24.2)	83/327 (25.4)	83/327 (25.4)	78/327 (23.9)	84/327 (25.7)	79/327 (24.2)	79/327 (24.2)	76/327 (23.2)
ACR20											
UPA	450/651 (69.1)	436/651 (67.0)	328/651 (50.4)	316/651 (48.5)	305/651 (46.9)	308/651 (47.3)	306/651 (47.0)	302/651 (46.4)	298/651 (45.8)	288/651 (44.2)	271/651 (41.6)
ADA	206/327 (63.0)	187/327 (57.2)	116/327 (35.5)	117/327 (35.8)	110/327 (33.6)	107/327 (32.7)	109/327 (33.3)	108/327 (33.0)	106/327 (32.4)	107/327 (32.7)	103/327 (31.5)
ACR50											
UPA	288/651 (44.2)	349/651 (53.6)	284/651 (43.6)	279/651 (42.9)	279/651 (42.9)	282/651 (43.3)	277/651 (42.5)	262/651 (40.2)	270/651 (41.5)	253/651 (38.9)	240/651 (36.9)
ADA	93/327 (28.4)	137/327 (41.9)	101/327 (30.9)	101/327 (30.9)	93/327 (28.4)	96/327 (29.4)	95/327 (29.1)	94/327 (28.7)	88/327 (26.9)	94/327 (28.7)	91/327 (27.8)
ACR70											
UPA	162/651 (24.9)	224/651 (34.4)	225/651 (34.6)	226/651 (34.7)	227/651 (34.9)	223/651 (34.3)	223/651 (34.3)	219/651 (33.6)	217/651 (33.3)	209/651 (32.1)	208/651 (32.0)
ADA	43/327 (13.1)	75/327 (22.9)	74/327 (22.6)	69/327 (21.1)	75/327 (22.9)	75/327 (22.9)	68/327 (20.8)	74/327 (22.6)	68/327 (20.8)	73/327 (22.3)	71/327 (21.7)
n/N (%)	Weeks										
	156	168	180	192	204	216	228	240	252	264	
CDAI ≤ 10											
UPA	257/651 (39.5)	262/651 (40.2)	260/651 (39.9)	252/651 (38.7)	241/651 (37.0)	252/651 (38.7)	243/651 (37.3)	245/651 (37.6)	238/651 (36.6)	237/651 (36.4)	
ADA	96/327 (29.4)	94/327 (28.7)	94/327 (28.7)	93/327 (28.4)	89/327 (27.2)	89/327 (27.2)	91/327 (27.8)	92/327 (28.1)	87/327 (26.6)	88/327 (26.9)	
CDAI ≤ 2.8											
UPA	159/651 (24.4)	164/651 (25.2)	165/651 (25.3)	171/651 (26.3)	166/651 (25.5)	165/651 (25.3)	168/651 (25.8)	157/651 (24.1)	160/651 (24.6)	160/651 (24.6)	
ADA	54/327 (16.5)	59/327 (18.0)	57/327 (17.4)	56/327 (17.1)	55/327 (16.8)	58/327 (17.7)	61/327 (18.7)	65/327 (19.9)	59/327 (18.0)	61/327 (18.7)	
DAS28(CRP) ≤ 3.2											
UPA	245/651 (37.6)	252/651 (38.7)	238/651 (36.6)	240/651 (36.9)	227/651 (34.9)	231/651 (35.5)	236/651 (36.3)	229/651 (35.2)	225/651 (34.6)	226/651 (34.7)	
ADA	85/327 (26.0)	78/327 (23.9)	78/327 (23.9)	83/327 (25.4)	78/327 (23.9)	75/327 (22.9)	79/327 (24.2)	83/327 (25.4)	76/327 (23.2)	81/327 (24.8)	
DAS28(CRP) < 2.6											
UPA	215/651 (33.0)	223/651 (34.3)	215/651 (33.0)	210/651 (32.3)	208/651 (32.0)	212/651 (32.6)	210/651 (32.3)	198/651 (30.4)	199/651 (30.6)	207/651 (31.8)	
ADA	71/327 (21.7)	73/327 (22.3)	63/327 (19.3)	69/327 (21.1)	64/327 (19.6)	64/327 (19.6)	67/327 (20.5)	75/327 (22.9)	67/327 (20.5)	76/327 (23.2)	
ACR20											
UPA	271/651 (41.6)	274/651 (42.1)	272/651 (41.8)	269/651 (41.3)	263/651 (40.4)	260/651 (39.9)	261/651 (40.1)	260/651 (39.9)	252/651 (38.7)	250/651 (38.4)	
ADA	98/327 (30.0)	100/327 (30.6)	99/327 (30.3)	99/327 (30.3)	94/327 (28.7)	95/327 (29.1)	96/327 (29.4)	94/327 (28.7)	92/327 (28.1)	93/327 (28.4)	

ACR50										
UPA	249/651 (38.2)	253/651 (38.9)	253/651 (38.9)	252/651 (38.7)	241/651 (37.0)	241/651 (37.0)	235/651 (36.1)	233/651 (35.8)	234/651 (35.9)	230/651 (35.3)
ADA	87/327 (26.6)	84/327 (25.7)	90/327 (27.5)	88/327 (26.9)	84/327 (25.7)	84/327 (25.7)	89/327 (27.2)	87/327 (26.6)	85/327 (26.0)	84/327 (25.7)
ACR70										
UPA	211/651 (32.4)	205/651 (31.5)	212/651 (32.6)	210/651 (32.3)	199/651 (30.6)	201/651 (30.9)	197/651 (30.3)	200/651 (30.7)	193/651 (29.6)	186/651 (28.6)
ADA	67/327 (20.5)	70/327 (21.4)	71/327 (21.7)	72/327 (22.0)	69/327 (21.1)	65/327 (19.9)	75/327 (22.9)	73/327 (22.3)	68/327 (20.8)	73/327 (22.3)

Categorical data points of categorical endpoints analysed by randomised treatment group (NRI) shown in Figure 1 (CDAI and DAS28[CRP] responses) and Figure 3 (ACR20/50/70 responses). ACR20/50/70, $\geq 20/50/70\%$ improvement in American College of Rheumatology response criteria; ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score based on C-reactive protein; LDA, low disease activity; NRI, non-responder imputation; UPA, upadacitinib.

Supplementary Table S9 Proportions of patients achieving CDAI LDA (≤ 10)/remission (≤ 2.8), DAS28(CRP) ≤ 3.2 / < 2.6 , ACR20, ACR50, ACR70 and no radiographic progression through 264 weeks (AO)											
n/N (%)	Weeks										
	12	26	48	60	72	84	96	108	120	132	144
CDAI ≤ 10											
UPA continued	232/367 (63.2)	334/359 (93.0)	301/343 (87.8)	303/338 (89.6)	297/328 (90.5)	294/326 (90.2)	288/322 (89.4)	279/310 (90.0)	282/309 (91.3)	276/308 (89.6)	271/290 (93.4)
ADA continued	77/147 (52.4)	122/137 (89.1)	111/131 (84.7)	111/130 (85.4)	108/125 (86.4)	102/127 (80.3)	100/123 (81.3)	105/120 (87.5)	103/116 (88.8)	104/114 (91.2)	100/114 (87.7)
PBO to UPA	108/613 (17.6)	264/600 (44.0)	383/571 (67.1)	387/553 (70.0)	401/539 (74.4)	400/532 (75.2)	394/515 (76.5)	399/506 (78.9)	411/495 (83.0)	396/488 (81.1)	372/456 (81.6)
ADA to UPA	22/157 (14.0)	31/154 (20.1)	82/143 (57.3)	82/139 (59.0)	84/132 (63.6)	82/129 (63.6)	81/127 (63.8)	81/124 (65.3)	88/125 (70.4)	95/125 (76.0)	85/115 (73.9)
UPA to ADA	34/246 (13.8)	36/248 (14.5)	102/229 (44.5)	115/217 (53.0)	107/204 (52.5)	123/200 (61.5)	110/190 (57.9)	113/183 (61.7)	108/176 (61.4)	113/180 (62.8)	112/176 (63.6)
CDAI ≤ 2.8											
UPA continued	87/367 (23.7)	150/359 (41.8)	167/343 (48.7)	161/338 (47.6)	184/328 (56.1)	177/326 (54.3)	177/322 (55.0)	164/310 (52.9)	170/309 (55.0)	172/308 (55.8)	160/290 (55.2)
ADA continued	24/147 (16.3)	45/137 (32.8)	55/131 (42.0)	51/130 (39.2)	55/125 (44.0)	56/127 (44.1)	53/123 (43.1)	54/120 (45.0)	54/116 (46.6)	56/114 (49.1)	62/114 (54.4)
PBO to UPA	20/613 (3.3)	71/600 (11.8)	160/571 (28.0)	170/553 (30.7)	191/539 (35.4)	197/532 (37.0)	203/515 (39.4)	191/506 (37.7)	203/495 (41.0)	208/488 (42.6)	191/456 (41.9)
ADA to UPA	1/157 (0.6)	6/154 (3.9)	26/143 (18.2)	33/139 (23.7)	27/132 (20.5)	28/129 (21.7)	25/127 (19.7)	35/124 (28.2)	38/125 (30.4)	32/125 (25.6)	35/115 (30.4)
UPA to ADA	0/246 (0)	4/248 (1.6)	13/229 (5.7)	22/217 (10.1)	26/204 (12.7)	32/200 (16.0)	32/190 (16.8)	31/183 (16.9)	30/176 (17.0)	31/180 (17.2)	34/176 (19.3)
DAS28(CRP) ≤ 3.2											
UPA continued	251/355 (70.7)	328/360 (91.1)	299/346 (86.4)	288/334 (86.2)	296/329 (90.0)	286/324 (88.3)	285/320 (89.1)	288/314 (91.7)	281/312 (90.1)	274/308 (89.0)	258/281 (91.8)
ADA continued	75/144 (52.1)	117/136 (86.0)	108/134 (80.6)	103/130 (79.2)	99/128 (77.3)	96/127 (75.6)	95/122 (77.9)	108/123 (87.8)	99/120 (82.5)	96/115 (83.5)	93/112 (83.0)
PBO to UPA	92/594 (15.5)	250/604 (41.4)	402/577 (69.7)	402/561 (71.7)	409/548 (74.6)	408/527 (77.4)	392/509 (77.0)	394/500 (78.8)	399/497 (80.3)	383/473 (81.0)	354/431 (82.1)
ADA to UPA	19/153 (12.4)	45/157 (28.7)	85/145 (58.6)	81/139 (58.3)	85/134 (63.4)	85/131 (64.9)	84/128 (65.6)	77/120 (64.2)	89/124 (71.8)	87/116 (75.0)	77/107 (72.0)
UPA to ADA	44/233 (18.9)	53/248 (21.4)	93/235 (39.6)	100/217 (46.1)	98/204 (48.0)	116/199 (58.3)	103/188 (54.8)	107/182 (58.8)	111/180 (61.7)	108/177 (61.0)	108/163 (66.3)
DAS28(CRP) < 2.6											
UPA continued	169/355 (47.6)	260/360 (72.2)	245/346 (70.8)	249/334 (74.6)	262/329 (79.6)	257/324 (79.3)	243/320 (75.9)	240/314 (76.4)	246/312 (78.8)	239/308 (77.6)	219/281 (77.9)
ADA continued	49/144 (34.0)	85/136 (62.5)	90/134 (67.2)	81/130 (62.3)	86/128 (67.2)	86/127 (67.7)	78/122 (63.9)	87/123 (70.7)	82/120 (68.3)	80/115 (69.6)	78/112 (69.6)
PBO to UPA	40/594 (6.7)	145/604 (24.0)	305/577 (52.9)	319/561 (56.9)	336/548 (61.3)	317/527 (60.2)	313/509 (61.5)	319/500 (63.8)	322/497 (64.8)	299/473 (63.2)	286/431 (66.4)
ADA to UPA	10/153 (6.5)	23/157 (14.6)	53/145 (36.6)	55/139 (39.6)	55/134 (41.0)	57/131 (43.5)	56/128 (43.8)	57/120 (47.5)	66/124 (53.2)	63/116 (54.3)	58/107 (54.2)
UPA to ADA	19/233 (8.2)	20/248 (8.1)	48/235 (20.4)	57/217 (26.3)	66/204 (32.4)	73/199 (36.7)	72/188 (38.3)	69/182 (37.9)	72/180 (40.0)	71/177 (40.1)	79/163 (48.5)
ACR20											
UPA continued	321/364 (88.2)	343/357 (96.1)	330/344 (95.9)	319/337 (94.7)	308/327 (94.2)	312/325 (96.0)	308/323 (95.4)	304/314 (96.8)	303/314 (96.5)	292/309 (94.5)	277/292 (94.9)
ADA continued	128/155 (82.6)	131/136 (96.3)	119/133 (89.5)	122/130 (93.8)	114/129 (88.4)	112/128 (87.5)	113/123 (91.9)	113/122 (92.6)	110/119 (92.4)	109/118 (92.4)	106/116 (91.4)
PBO to UPA	236/616 (38.3)	447/598 (74.7)	502/577 (87.0)	481/564 (85.3)	481/548 (87.8)	473/537 (88.1)	471/518 (90.9)	459/512 (89.6)	464/501 (92.6)	447/484 (92.4)	418/459 (91.1)
ADA to UPA	81/155 (52.3)	111/155 (71.6)	117/143 (81.8)	119/136 (87.5)	121/134 (90.3)	112/129 (86.8)	121/129 (93.8)	114/127 (89.8)	110/124 (88.7)	107/120 (89.2)	103/114 (90.4)
UPA to ADA	131/243 (53.9)	152/242 (62.8)	169/229 (73.8)	173/218 (79.4)	161/202 (79.7)	162/200 (81.0)	158/191 (82.7)	143/185 (77.3)	149/182 (81.9)	147/180 (81.7)	148/174 (85.1)
ACR50											
UPA continued	241/367 (65.7)	311/356 (87.4)	285/342 (83.3)	281/332 (84.6)	281/329 (85.4)	285/325 (87.7)	277/321 (86.3)	264/312 (84.6)	275/314 (87.6)	256/305 (83.9)	242/292 (82.9)
ADA continued	75/152 (49.3)	109/136 (80.1)	103/132 (78.0)	103/132 (78.0)	96/129 (74.4)	99/128 (77.3)	97/125 (77.6)	97/123 (78.9)	92/120 (76.7)	96/118 (81.4)	93/115 (80.9)
PBO to UPA	97/619 (15.7)	272/601 (45.3)	373/576 (64.8)	374/563 (66.4)	387/546 (70.9)	381/529 (72.0)	374/518 (72.2)	378/507 (74.6)	372/495 (75.2)	361/481 (75.1)	346/456 (75.9)
ADA to UPA	19/157 (12.1)	60/154 (39.0)	83/141 (58.9)	87/137 (63.5)	94/134 (70.1)	85/130 (65.4)	87/128 (68.0)	81/125 (64.8)	91/123 (74.0)	80/119 (67.2)	79/112 (70.5)
UPA to ADA	49/246 (19.9)	66/243 (27.2)	96/232 (41.4)	111/216 (51.4)	97/202 (48.0)	107/200 (53.5)	98/189 (51.9)	107/179 (59.8)	105/180 (58.3)	99/178 (55.6)	105/171 (61.4)
ACR70											
UPA continued	152/371 (41.0)	215/354 (60.7)	226/342 (66.1)	227/336 (67.6)	228/328 (69.5)	224/324 (69.1)	223/324 (68.8)	221/312 (70.8)	218/314 (69.4)	211/306 (69.0)	210/290 (72.4)

ADA continued	38/151 (25.2)	73/135 (54.1)	75/131 (57.3)	71/131 (54.2)	77/129 (59.7)	75/124 (60.5)	70/123 (56.9)	75/122 (61.5)	72/120 (60.0)	74/117 (63.2)	73/115 (63.5)
PBO to UPA	32/624 (5.1)	121/604 (20.0)	246/576 (42.7)	256/561 (45.6)	284/547 (51.9)	273/537 (50.8)	293/517 (56.7)	271/504 (53.8)	278/495 (56.2)	276/483 (57.1)	259/453 (57.2)
ADA to UPA	5/158 (3.2)	15/154 (9.7)	52/142 (36.6)	50/139 (36.0)	56/134 (41.8)	58/129 (45.0)	56/126 (44.4)	50/123 (40.7)	60/124 (48.4)	56/119 (47.1)	54/111 (48.6)
UPA to ADA	11/250 (4.4)	16/245 (6.5)	43/233 (18.5)	63/220 (28.6)	53/204 (26.0)	60/199 (30.2)	65/191 (34.0)	60/182 (33.0)	65/181 (35.9)	58/180 (32.2)	60/173 (34.7)
Δ mTSS ≤ 0											
UPA continued	—	254/282 (90.1)	—	—	—	—	—	243/292 (83.2)	—	—	—
ADA continued	—	99/112 (88.4)	—	—	—	—	—	93/114 (81.6)	—	—	—
PBO to UPA	—	367/435 (84.4)	—	—	—	—	—	358/446 (80.3)	—	—	—
ADA to UPA	—	97/112 (86.6)	—	—	—	—	—	94/113 (83.2)	—	—	—
UPA to ADA	—	126/150 (84.0)	—	—	—	—	—	115/152 (75.7)	—	—	—
Weeks											
n/N (%)	156	168	180	192	204	216	228	240	252	264	
CDAI ≤ 10											
UPA continued	260/281 (92.5)	266/287 (92.7)	263/287 (91.6)	256/283 (90.5)	246/278 (88.5)	258/277 (93.1)	248/275 (90.2)	250/266 (94.0)	241/263 (91.6)	244/260 (93.8)	
ADA continued	100/109 (91.7)	99/110 (90.0)	99/110 (90.0)	98/109 (89.9)	97/108 (89.8)	91/105 (86.7)	94/103 (91.3)	97/104 (93.3)	89/95 (93.7)	92/98 (93.9)	
PBO to UPA	357/440 (81.1)	367/444 (82.7)	364/434 (83.9)	359/436 (82.3)	359/438 (82.0)	360/430 (83.7)	357/431 (82.8)	358/422 (84.8)	338/414 (81.6)	331/415 (79.8)	
ADA to UPA	84/114 (73.7)	87/111 (78.4)	78/109 (71.6)	82/110 (74.5)	83/110 (75.5)	86/108 (79.6)	79/106 (74.5)	79/101 (78.2)	78/102 (76.5)	82/100 (82.0)	
UPA to ADA	101/157 (64.3)	101/159 (63.5)	103/151 (68.2)	100/153 (65.4)	102/147 (69.4)	98/141 (69.5)	101/144 (70.1)	96/142 (67.6)	100/136 (73.5)	103/137 (75.2)	
CDAI ≤ 2.8											
UPA continued	159/281 (56.6)	164/287 (57.1)	166/287 (57.8)	171/283 (60.4)	167/278 (60.1)	167/277 (60.3)	171/275 (62.2)	158/266 (59.4)	160/263 (60.8)	162/260 (62.3)	
ADA continued	57/109 (52.3)	62/110 (56.4)	59/110 (53.6)	58/109 (53.2)	59/108 (54.6)	60/105 (57.1)	62/103 (60.2)	68/104 (65.4)	61/95 (64.2)	64/98 (65.3)	
PBO to UPA	203/440 (46.1)	199/444 (44.8)	186/434 (42.9)	185/436 (42.4)	197/438 (45.0)	188/430 (43.7)	185/431 (42.9)	194/422 (46.0)	166/414 (40.1)	181/415 (43.6)	
ADA to UPA	34/114 (29.8)	37/111 (33.3)	35/109 (32.1)	34/110 (30.9)	32/110 (29.1)	33/108 (30.6)	34/106 (32.1)	38/101 (37.6)	31/102 (30.4)	32/100 (32.0)	
UPA to ADA	36/157 (22.9)	33/159 (20.8)	37/151 (24.5)	39/153 (25.5)	30/147 (20.4)	36/141 (25.5)	34/144 (23.6)	38/142 (26.8)	38/136 (27.9)	36/137 (26.3)	
DAS28(CRP) ≤ 3.2											
UPA continued	247/265 (93.2)	255/269 (94.8)	241/260 (92.7)	244/264 (92.4)	232/259 (89.6)	238/258 (92.2)	242/268 (90.3)	232/252 (92.1)	229/253 (90.5)	233/249 (93.6)	
ADA continued	89/100 (89.0)	82/96 (85.4)	82/95 (86.3)	89/103 (86.4)	85/98 (86.7)	77/94 (81.9)	82/92 (89.1)	88/97 (90.7)	79/89 (88.8)	85/95 (89.5)	
PBO to UPA	331/405 (81.7)	323/401 (80.5)	320/399 (80.2)	340/413 (82.3)	328/408 (80.4)	326/394 (82.7)	335/412 (81.3)	338/402 (84.1)	310/384 (80.7)	307/388 (79.1)	
ADA to UPA	78/106 (73.6)	79/99 (79.8)	68/95 (71.6)	79/105 (75.2)	73/101 (72.3)	79/100 (79.0)	76/102 (74.5)	70/96 (72.9)	73/94 (77.7)	81/93 (87.1)	
UPA to ADA	92/152 (60.5)	90/148 (60.8)	95/145 (65.5)	96/145 (66.2)	89/135 (65.9)	92/134 (68.7)	99/139 (71.2)	94/138 (68.1)	91/130 (70.0)	96/131 (73.3)	
DAS28(CRP) < 2.6											
UPA continued	216/265 (81.5)	224/269 (83.3)	217/260 (83.5)	213/264 (80.7)	213/259 (82.2)	216/258 (83.7)	214/268 (79.9)	200/252 (79.4)	202/253 (79.8)	211/249 (84.7)	
ADA continued	73/100 (73.0)	76/96 (79.2)	66/95 (69.5)	73/103 (70.9)	68/98 (69.4)	66/94 (70.2)	68/92 (73.9)	79/97 (81.4)	69/89 (77.5)	80/95 (84.2)	
PBO to UPA	267/405 (65.9)	259/401 (64.6)	263/399 (65.9)	276/413 (66.8)	271/408 (66.4)	271/394 (68.8)	280/412 (68.0)	282/402 (70.1)	255/384 (66.4)	261/388 (67.3)	
ADA to UPA	60/106 (56.6)	58/99 (58.6)	57/95 (60.0)	55/105 (52.4)	56/101 (55.4)	56/100 (56.0)	61/102 (59.8)	57/96 (59.4)	52/94 (55.3)	53/93 (57.0)	
UPA to ADA	68/152 (44.7)	62/148 (41.9)	71/145 (49.0)	74/145 (51.0)	65/135 (48.1)	64/134 (47.8)	66/139 (47.5)	66/138 (47.8)	64/130 (49.2)	68/131 (51.9)	
ACR20											
UPA continued	272/283 (96.1)	278/287 (96.9)	276/285 (96.8)	272/283 (96.1)	270/278 (97.1)	266/276 (96.4)	266/279 (95.3)	264/271 (97.4)	254/266 (95.5)	256/264 (97.0)	
ADA continued	102/109 (93.6)	105/111 (94.6)	105/110 (95.5)	107/113 (94.7)	102/109 (93.6)	100/104 (96.2)	100/104 (96.2)	102/105 (97.1)	94/98 (95.9)	97/101 (96.0)	
PBO to UPA	404/442 (91.4)	394/445 (88.5)	401/438 (91.6)	403/445 (90.6)	399/440 (90.7)	392/429 (91.4)	394/435 (90.6)	389/426 (91.3)	377/418 (90.2)	374/414 (90.3)	
ADA to UPA	101/115 (87.8)	101/109 (92.7)	95/104 (91.3)	99/111 (89.2)	97/109 (89.0)	99/107 (92.5)	96/107 (89.7)	95/102 (93.1)	90/99 (90.9)	89/99 (89.9)	
UPA to ADA	136/163 (83.4)	127/159 (79.9)	136/154 (88.3)	133/152 (87.5)	123/145 (84.8)	124/144 (86.1)	117/148 (79.1)	122/147 (83.0)	117/138 (84.8)	121/139 (87.1)	
ACR50											
UPA continued	250/284 (88.0)	254/286 (88.8)	254/284 (89.4)	253/285 (88.8)	244/280 (87.1)	245/275 (89.1)	239/277 (86.3)	234/269 (87.0)	236/268 (88.1)	234/262 (89.3)	
ADA continued	91/111 (82.0)	88/110 (80.0)	95/110 (86.4)	95/113 (84.1)	91/109 (83.5)	86/104 (82.7)	93/104 (89.4)	93/105 (88.6)	87/99 (87.9)	87/101 (86.1)	

PBO to UPA	326/434 (75.1)	333/436 (76.4)	331/432 (76.6)	331/439 (75.4)	323/429 (75.3)	329/427 (77.0)	328/430 (76.3)	326/421 (77.4)	306/415 (73.7)	302/410 (73.7)
ADA to UPA	85/114 (74.6)	83/107 (77.6)	76/104 (73.1)	76/110 (69.1)	75/107 (70.1)	80/105 (76.2)	79/105 (75.2)	75/100 (75.0)	71/99 (71.7)	71/98 (72.4)
UPA to ADA	93/159 (58.5)	92/159 (57.9)	99/155 (63.9)	91/151 (60.3)	90/145 (62.1)	84/141 (59.6)	84/145 (57.9)	85/143 (59.4)	93/136 (68.4)	88/139 (63.3)
ACR70										
UPA continued	211/285 (74.0)	205/287 (71.4)	213/284 (75.0)	211/284 (74.3)	201/278 (72.3)	203/277 (73.3)	199/279 (71.3)	201/272 (73.9)	194/269 (72.1)	189/258 (73.3)
ADA continued	71/107 (66.4)	73/109 (67.0)	74/108 (68.5)	75/111 (67.6)	74/107 (69.2)	67/104 (64.4)	76/102 (74.5)	76/103 (73.8)	70/97 (72.2)	76/98 (77.6)
PBO to UPA	257/436 (58.9)	246/439 (56.0)	254/430 (59.1)	263/441 (59.6)	244/428 (57.0)	251/423 (59.3)	250/428 (58.4)	258/424 (60.8)	236/414 (57.0)	241/408 (59.1)
ADA to UPA	60/113 (53.1)	53/109 (48.6)	57/106 (53.8)	56/109 (51.4)	53/107 (49.5)	54/104 (51.9)	51/101 (50.5)	50/98 (51.0)	47/99 (47.5)	50/98 (51.0)
UPA to ADA	54/162 (33.3)	55/156 (35.3)	61/152 (40.1)	59/153 (38.6)	61/145 (42.1)	56/141 (39.7)	53/146 (36.3)	60/142 (42.3)	50/133 (37.6)	60/137 (43.8)
Δ mTSS ≤ 0										
UPA continued	—	—	—	233/288 (80.9)	—	—	—	—	—	—
ADA continued	—	—	—	85/109 (78.0)	—	—	—	—	—	—
PBO to UPA	—	—	—	341/442 (77.1)	—	—	—	—	—	—
ADA to UPA	—	—	—	86/111 (77.5)	—	—	—	—	—	—
UPA to ADA	—	—	—	111/150 (74.0)	—	—	—	—	—	—

Categorical data points of categorical endpoints analysed by treatment sequence AO, without imputation for missing data shown in Figure 2 (CDAI and

DAS28[CRP] responses), Figure 4 (ACR20/50/70 responses) and Figure 5 (radiographic outcomes). Δ , change from baseline; ACR20/50/70, $\geq 20/50/70\%$

improvement in American College of Rheumatology response criteria; ADA, adalimumab; AO, as observed; CDAI, Clinical Disease Activity Index; DAS28(CRP),

28-joint Disease Activity Score based on C-reactive protein; LDA, low disease activity; mTSS, modified Total Sharp Score; PBO, placebo; UPA, upadacitinib.

Supplementary Table S10 Mean change from BL in core components of ACR criteria and mTSS through 264 weeks (AO)

n/N (mean change from BL)	Weeks										
	12	26	48	60	72	84	96	108	120	132	144
TJC68											
UPA continued	374/399 (-18.6)	360/399 (-21.6)	347/399 (-21.5)	342/399 (-21.7)	334/399 (-21.9)	329/399 (-21.7)	327/399 (-21.8)	321/399 (-21.8)	319/399 (-21.9)	314/399 (-21.7)	297/399 (-21.9)
ADA continued	155/168 (-17.6)	137/168 (-20.9)	134/168 (-20.6)	132/168 (-21.2)	130/168 (-21.1)	128/168 (-20.7)	127/168 (-21.1)	124/168 (-20.9)	122/168 (-21.4)	118/168 (-21.1)	117/168 (-21.1)
PBO to UPA	625/650 (-9.7)	607/650 (-17.5)	582/650 (-20.9)	570/650 (-21.7)	553/650 (-22.3)	540/650 (-22.5)	527/650 (-22.7)	516/650 (-22.8)	505/650 (-23.2)	491/650 (-23.4)	469/650 (-23.6)
ADA to UPA	159/159 (-11.6)	157/159 (-16.6)	146/159 (-21.0)	142/159 (-22.2)	138/159 (-23.5)	134/159 (-23.1)	131/159 (-23.0)	128/159 (-23.6)	126/159 (-24.0)	125/159 (-24.2)	117/159 (-24.8)
UPA to ADA	250/252 (-13.8)	248/252 (-17.9)	237/248 (-21.9)	223/252 (-23.0)	207/252 (-23.8)	203/252 (-24.2)	194/252 (-24.4)	186/252 (-24.8)	185/252 (-25.0)	183/252 (-24.5)	178/252 (-24.9)
SJC66											
UPA continued	374/399 (-13.2)	360/399 (-14.8)	347/399 (-14.9)	342/399 (-14.9)	334/399 (-15.0)	329/399 (-14.8)	327/399 (-15.0)	321/399 (-14.9)	319/399 (-14.8)	314/399 (-14.8)	297/399 (-15.0)
ADA continued	155/168 (-11.8)	137/168 (-13.8)	134/168 (-13.6)	132/168 (-13.9)	130/168 (-13.7)	128/168 (-13.5)	127/168 (-13.6)	124/168 (-13.7)	122/168 (-13.4)	118/168 (-13.4)	117/168 (-13.3)
PBO to UPA	625/650 (-7.0)	607/650 (-11.7)	582/650 (-13.6)	570/650 (-14.0)	553/650 (-14.5)	540/650 (-14.5)	527/650 (-14.7)	516/650 (-14.5)	505/650 (-14.9)	491/650 (-15.0)	469/650 (-15.1)
ADA to UPA	159/159 (-9.0)	157/159 (-12.3)	146/159 (-14.4)	142/159 (-14.6)	138/159 (-15.4)	134/159 (-14.8)	131/159 (-15.2)	128/159 (-15.4)	126/159 (-15.8)	125/159 (-16.0)	117/159 (-16.2)
UPA to ADA	250/252 (-9.0)	248/252 (-11.4)	237/252 (-13.8)	223/252 (-13.7)	207/252 (-14.1)	203/252 (-14.3)	194/252 (-14.4)	186/252 (-14.7)	185/252 (-14.6)	183/252 (-14.7)	178/252 (-14.9)
PtGA											
UPA continued	373/397 (-36.7)	358/397 (-46.1)	345/397 (-46.4)	339/397 (-45.9)	331/397 (-46.7)	327/397 (-47.2)	325/397 (-46.7)	318/397 (-46.3)	317/397 (-47.8)	310/397 (-47.5)	293/397 (-47.6)
ADA continued	155/168 (-29.1)	137/168 (-41.9)	134/168 (-42.7)	132/168 (-41.5)	130/168 (-42.1)	128/168 (-41.1)	125/168 (-41.0)	124/168 (-44.4)	123/168 (-41.4)	118/168 (-45.3)	117/168 (-45.2)
PBO to UPA	622/648 (-15.5)	605/648 (-30.2)	579/648 (-37.3)	566/648 (-37.8)	551/648 (-40.2)	539/648 (-40.8)	524/648 (-41.3)	512/648 (-41.5)	501/648 (-43.1)	489/648 (-42.8)	463/648 (-42.7)
ADA to UPA	157/157 (-20.7)	156/157 (-28.9)	145/157 (-38.6)	140/157 (-38.5)	137/157 (-40.1)	132/157 (-40.1)	129/157 (-44.0)	127/157 (-40.6)	125/157 (-43.4)	124/157 (-42.0)	116/157 (-45.4)
UPA to ADA	247/250 (-21.9)	246/250 (-23.8)	233/250 (-30.2)	220/250 (-32.0)	205/250 (-31.9)	201/248 (-35.5)	193/250 (-35.7)	185/250 (-35.3)	183/250 (-35.4)	182/250 (-36.0)	176/250 (-36.7)
PhGA											
UPA continued	347/375 (-45.5)	339/375 (-54.7)	324/375 (-55.2)	320/375 (-55.7)	311/375 (-56.1)	309/375 (-56.5)	307/375 (-57.0)	295/375 (-56.1)	294/375 (-57.0)	293/375 (-56.5)	277/375 (-56.7)
ADA continued	141/160 (-39.5)	132/160 (-48.9)	126/160 (-50.9)	125/160 (-51.1)	120/160 (-52.6)	122/160 (-52.2)	120/160 (-51.5)	116/160 (-53.3)	114/160 (-51.7)	110/160 (-52.3)	110/160 (-53.7)
PBO to UPA	588/619 (-25.3)	573/619 (-41.8)	544/619 (-51.0)	528/619 (-52.3)	513/619 (-53.7)	508/619 (-54.3)	489/619 (-55.1)	480/619 (-54.8)	470/619 (-55.8)	461/619 (-56.6)	430/619 (-56.4)

ADA to UPA	144/145 (-32.5)	142/145 (-40.7)	131/145 (-48.7)	127/145 (-51.2)	122/145 (-53.7)	118/145 (-53.2)	117/145 (-54.8)	112/145 (-54.0)	112/145 (-53.9)	112/145 (-54.3)	103/145 (-55.2)
UPA to ADA	235/241 (-29.4)	237/241 (-35.6)	219/241 (-42.0)	207/241 (-45.3)	195/241 (-46.0)	193/241 (-49.1)	184/241 (-47.8)	177/241 (-48.2)	170/241 (-51.2)	173/241 (-49.5)	170/241 (-48.2)
Pain											
UPA continued	373/397 (-37.8)	358/397 (-46.1)	345/397 (-46.6)	339/397 (-46.5)	331/397 (-47.1)	327/397 (-48.1)	325/397 (-47.4)	318/397 (-47.6)	317/397 (-47.9)	310/397 (-47.3)	293/397 (-47.7)
ADA continued	155/168 (-31.5)	137/168 (-44.1)	134/168 (-43.8)	132/168 (-42.5)	130/168 (-42.3)	128/168 (-42.1)	125/168 (-42.6)	124/168 (-44.1)	123/168 (-42.9)	118/168 (-44.8)	117/168 (-44.7)
PBO to UPA	622/648 (-15.6)	605/648 (-31.4)	579/648 (-39.3)	566/648 (-39.4)	551/648 (-41.5)	539/648 (-41.9)	524/648 (-41.9)	512/648 (-42.5)	501/648 (-43.2)	489/648 (-43.0)	463/648 (-43.1)
ADA to UPA	157/157 (-21.2)	156/157 (-28.9)	145/157 (-39.3)	140/157 (-38.1)	137/157 (-41.4)	132/157 (-40.8)	130/157 (-44.3)	127/157 (-41.2)	125/157 (-41.3)	124/157 (-41.7)	116/157 (-43.4)
UPA to ADA	247/250 (-24.1)	246/250 (-26.2)	233/250 (-32.5)	220/250 (-34.3)	205/250 (-33.3)	201/250 (-36.4)	193/250 (-37.9)	185/250 (-38.2)	183/250 (-38.7)	182/250 (-37.7)	176/250 (-39.2)
HAQ-DI											
UPA continued	373/397 (-0.80)	358/397 (-0.93)	345/397 (-0.99)	339/397 (-0.98)	331/397 (-1.00)	327/397 (-1.02)	325/397 (-1.01)	318/397 (-1.01)	316/397 (-1.02)	310/397 (-1.00)	293/397 (-1.01)
ADA continued	155/168 (-0.63)	137/168 (-0.79)	134/168 (-0.79)	132/168 (-0.84)	130/168 (-0.83)	128/168 (-0.78)	125/168 (-0.82)	124/168 (-0.84)	123/168 (-0.82)	118/168 (-0.79)	117/168 (-0.83)
PBO to UPA	622/648 (-0.32)	604/648 (-0.59)	579/648 (-0.76)	566/648 (-0.77)	551/648 (-0.81)	539/648 (-0.82)	524/648 (-0.84)	512/648 (-0.82)	501/648 (-0.86)	488/648 (-0.84)	463/648 (-0.86)
ADA to UPA	157/157 (-0.46)	156/157 (-0.60)	145/157 (-0.75)	140/157 (-0.98)	137/157 (-0.84)	132/157 (-0.79)	130/157 (-0.84)	127/157 (-0.84)	125/157 (-0.84)	124/157 (-0.84)	116/157 (-0.91)
UPA to ADA	246/249 (-0.43)	245/249 (-0.51)	232/249 (-0.59)	219/249 (-0.67)	204/249 (-0.67)	200/249 (-0.70)	192/249 (-0.73)	184/249 (-0.73)	181/249 (-0.75)	181/249 (-0.70)	175/249 (-0.71)
hsCRP											
UPA continued	357/399 (-12.9)	361/399 (-13.8)	346/399 (-12.2)	335/399 (-12.3)	330/399 (-13.2)	324/399 (-13.8)	320/399 (-12.3)	315/399 (-13.6)	312/399 (-13.1)	310/399 (-12.9)	283/399 (-13.5)
ADA continued	146/167 (-8.4)	137/167 (-10.4)	134/167 (-9.3)	130/167 (-8.0)	128/167 (-9.5)	127/167 (-8.2)	124/167 (-9.1)	123/167 (-9.2)	121/167 (-8.8)	115/167 (-7.0)	112/167 (-7.9)
PBO to UPA	595/650 (-1.8)	605/650 (-8.1)	578/650 (-11.9)	563/650 (-13.1)	550/650 (-12.4)	527/650 (-12.2)	510/650 (-12.6)	502/650 (-13.9)	499/650 (-12.9)	474/650 (-13.4)	435/650 (-13.5)
ADA to UPA	153/159 (-12.5)	157/159 (-15.1)	146/159 (-17.1)	140/159 (-17.6)	134/159 (-17.5)	132/159 (-16.8)	129/159 (-15.8)	120/159 (-17.1)	124/159 (-17.1)	116/159 (-17.8)	108/159 (-18.7)
UPA to ADA	233/252 (-12.4)	248/252 (-12.1)	237/252 (-10.4)	219/252 (-9.9)	206/252 (-10.7)	201/252 (-10.6)	188/252 (-10.2)	182/252 (-9.7)	181/252 (-10.5)	177/252 (-12.5)	164/252 (-12.6)
ΔmTSS											
UPA continued	—	282 (0.14)	—	—	—	—	292 (0.37)	—	—	—	—
ADA continued	—	112 (0.04)	—	—	—	—	114 (0.43)	—	—	—	—
PBO to UPA	—	435 (0.37)	—	—	—	—	446 (0.70)	—	—	—	—
ADA to UPA	—	112 (0.17)	—	—	—	—	113 (0.63)	—	—	—	—
UPA to ADA	—	150 (0.33)	—	—	—	—	152 (1.03)	—	—	—	—
Severity of morning stiffness											

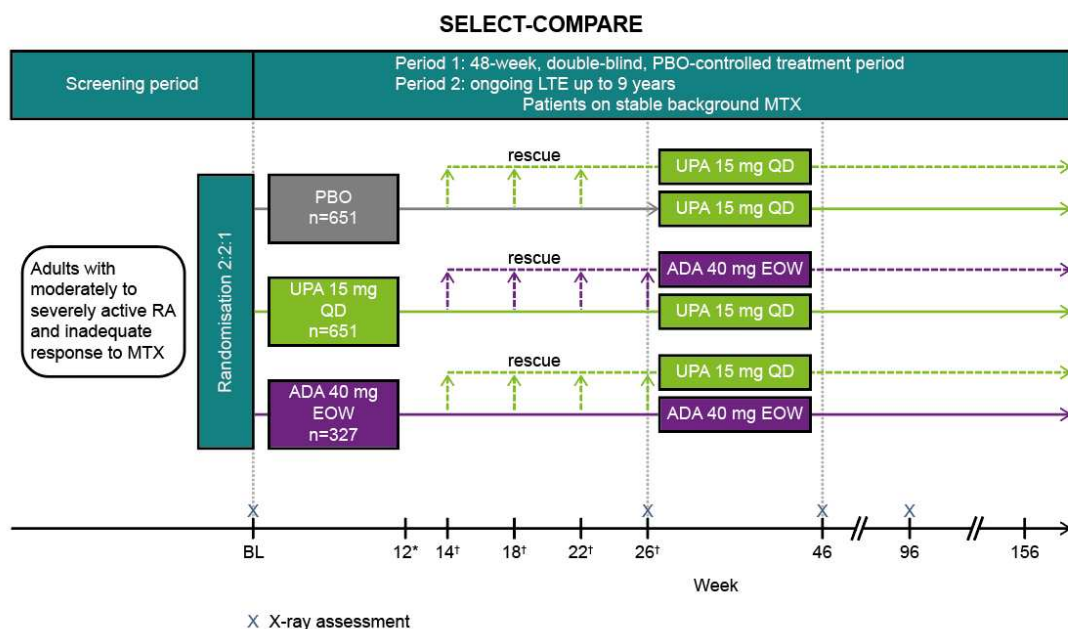
(0–10 NRS)											
UPA continued	374/399 (-4.2)	360/399 (-4.9)	347/399 (-4.9)	342/399 (-5.0)	333/399 (-5.0)	328/399 (-5.1)	325/399 (-5.2)	320/399 (-5.2)	317/399 (-5.1)	313/399 (-5.0)	299/399 (-5.1)
ADA continued	154/167 (-3.4)	135/167 (-4.3)	133/167 (-4.6)	131/167 (-4.5)	129/167 (-4.5)	127/167 (-4.5)	125/167 (-4.5)	123/167 (-4.7)	122/167 (-4.5)	117/167 (-4.6)	117/167 (-4.6)
PBO to UPA	625/650 (-1.9)	607/650 (-3.4)	581/650 (-4.4)	563/650 (-4.4)	554/650 (-4.6)	540/650 (-4.6)	525/650 (-4.7)	516/650 (-4.7)	504/650 (-4.8)	491/650 (-4.8)	470/650 (-4.9)
ADA to UPA	157/157 (-2.5)	155/157 (-3.5)	143/157 (-4.0)	139/157 (-4.3)	136/157 (-4.6)	130/157 (-4.4)	129/157 (-4.8)	126/157 (-4.6)	125/157 (-4.6)	123/157 (-4.6)	116/157 (-4.7)
UPA to ADA	248/249 (-2.5)	246/249 (-3.1)	234/249 (-3.6)	219/249 (-3.7)	204/249 (-3.8)	200/249 (-3.9)	191/249 (-3.9)	183/249 (-4.0)	183/249 (-4.1)	180/249 (-4.1)	177/249 (-4.2)
Duration of morning stiffness (mins)											
UPA continued	375/399 (-112.5)	360/399 (-125.0)	347/399 (-127.7)	342/399 (-121.9)	333/399 (-128.0)	328/399 (-131.7)	327/399 (-131.5)	320/399 (-132.4)	319/399 (-130.8)	314/399 (-131.3)	297/399 (-132.8)
ADA continued	154/167 (-83.5)	136/167 (-101.5)	133/167 (-103.6)	131/167 (-95.3)	129/167 (-96.5)	127/167 (-85.9)	125/167 (-98.9)	123/167 (-87.0)	122/167 (-86.0)	177/167 (-87.1)	114/167 (-98.6)
PBO to UPA	625/650 (-51.8)	607/650 (-89.5)	582/650 (-112.9)	565/650 (-111.4)	554/650 (-116.7)	541/650 (-117.9)	526/650 (-122.4)	516/650 (-120.8)	505/650 (-122.0)	491/650 (-124.9)	456/650 (-131.3)
ADA to UPA	157/157 (-91.7)	155/157 (-111.4)	144/157 (-125.0)	140/157 (-133.4)	136/157 (-132.8)	131/157 (-137.8)	129/157 (-141.4)	126/157 (-135.2)	125/157 (-144.6)	124/157 (-144.2)	116/157 (-152.7)
UPA to ADA	249/250 (-62.6)	247/250 (-67.0)	236/250 (-93.6)	221/250 (-101.9)	206/250 (-101.6)	200/250 (-100.9)	193/250 (-96.4)	184/250 (-100.4)	184/250 (-106.0)	181/250 (-110.4)	164/250 (-109.9)
Weeks											
n/N (mean change from BL)	156	168	180	192	204	216	228	240	252	264	
TJC68											
UPA continued	291/399 (-21.8)	293/399 (-22.2)	290/399 (-21.7)	289/399 (-21.6)	284/399 (-21.6)	281/399 (-21.8)	282/399 (-21.6)	277/399 (-21.8)	275/399 (-21.4)	269/399 (-22.1)	
ADA continued	113/168 (-21.5)	112/168 (-21.7)	112/168 (-21.1)	113/168 (-21.2)	109/168 (-21.5)	106/168 (-21.4)	105/168 (-21.9)	106/168 (-21.9)	101/168 (-22.0)	101/168 (-22.0)	
PBO to UPA	448/650 (-23.5)	456/650 (-23.4)	450/650 (-23.6)	453/650 (-23.5)	445/650 (-23.7)	439/650 (-23.7)	441/650 (-23.7)	431/650 (-23.4)	426/650 (-23.2)	422/650 (-23.5)	
ADA to UPA	117/159 (-24.8)	114/159 (-25.8)	110/159 (-25.6)	113/159 (-25.0)	111/159 (-25.6)	109/159 (-25.8)	108/159 (-26.0)	103/159 (-26.1)	103/159 (-26.2)	100/159 (-25.9)	
UPA to ADA	164/252 (-24.7)	162/252 (-24.9)	157/252 (-25.5)	155/252 (-25.8)	149/252 (-26.5)	145/252 (-26.7)	147/252 (-26.5)	149/252 (-26.4)	143/252 (-27.3)	141/252 (-27.6)	
SIC66											
UPA continued	291/399 (-15.0)	293/399 (-15.1)	290/399 (-14.7)	289/399 (-14.9)	284/399 (-14.6)	281/399 (-14.9)	282/399 (-14.8)	277/399 (-14.8)	275/399 (-14.5)	269/399 (-15.0)	
ADA continued	113/168 (-13.6)	112/168 (-13.8)	112/168 (-13.7)	113/168 (-13.1)	109/168 (-13.9)	106/168 (-13.4)	105/168 (-13.6)	106/168 (-13.7)	101/168 (-13.6)	101/168 (-13.5)	
PBO to UPA	448/650 (-14.9)	456/650 (-14.9)	450/650 (-15.0)	453/650 (-15.0)	445/650 (-15.3)	439/650 (-15.2)	441/650 (-15.2)	431/650 (-15.2)	426/650 (-15.2)	422/650 (-15.1)	

ADA to UPA	117/159 (-16.3)	114/159 (-16.6)	110/159 (-16.4)	113/159 (-16.0)	111/159 (-16.5)	109/159 (-16.9)	108/159 (-16.3)	103/159 (-16.8)	103/159 (-16.9)	100/159 (-16.9)
UPA to ADA	164/252 (-14.4)	162/252 (-14.8)	157/252 (-15.4)	155/252 (-15.2)	149/252 (-15.4)	145/252 (-15.4)	147/252 (-15.6)	149/252 (-15.5)	143/252 (-16.0)	141/252 (-16.2)
PtGA										
UPA continued	288/397 (-48.4)	289/397 (-48.9)	289/397 (-48.4)	286/397 (-48.6)	281/397 (-48.2)	279/397 (-48.2)	280/397 (-47.5)	273/397 (-47.8)	271/397 (-47.4)	265/397 (-48.9)
ADA continued	112/168 (-44.4)	112/168 (-45.7)	111/168 (-47.6)	113/168 (-47.8)	109/168 (-47.0)	106/168 (-45.7)	105/168 (-49.4)	105/168 (-49.5)	99/168 (-48.1)	101/168 (-47.9)
PBO to UPA	445/648 (-43.6)	450/648 (-42.8)	441/648 (-44.2)	447/648 (-43.7)	440/648 (-43.0)	433/648 (-44.2)	437/648 (-43.2)	428/648 (-44.0)	419/648 (-42.8)	417/648 (-42.6)
ADA to UPA	115/157 (-45.6)	111/157 (-45.0)	109/157 (-47.3)	112/157 (-43.5)	109/157 (-44.7)	107/157 (-45.9)	107/157 (-45.0)	102/157 (-45.6)	101/157 (-42.8)	99/157 (-45.5)
UPA to ADA	164/250 (-35.7)	161/250 (-36.0)	156/250 (-37.5)	154/250 (-36.9)	147/250 (-37.8)	145/250 (-37.2)	148/250 (-34.8)	148/250 (-38.3)	139/250 (-38.9)	140/250 (-38.5)
PhGA										
UPA continued	268/375 (-56.8)	275/375 (-56.0)	273/375 (-56.1)	269/375 (-55.1)	266/375 (-55.0)	264/375 (-56.2)	262/375 (-55.6)	256/375 (-56.7)	251/375 (-55.5)	247/375 (-56.7)
ADA continued	105/160 (-54.2)	106/160 (-53.7)	106/160 (-53.8)	106/160 (-53.5)	104/160 (-53.0)	101/160 (-52.5)	99/160 (-55.0)	100/160 (-52.5)	92/160 (-55.1)	94/160 (-53.7)
PBO to UPA	418/619 (-56.4)	420/619 (-57.1)	411/619 (-56.6)	410/619 (-56.1)	412/619 (-56.6)	408/619 (-56.1)	409/619 (-56.1)	399/619 (-56.3)	392/619 (-55.1)	393/619 (-54.3)
ADA to UPA	102/145 (-55.9)	102/145 (-56.2)	99/145 (-56.6)	99/145 (-55.2)	99/145 (-55.9)	98/145 (-54.6)	96/145 (-54.9)	92/145 (-57.5)	92/145 (-56.8)	90/145 (-56.4)
UPA to ADA	152/241 (-51.0)	153/241 (-50.3)	145/241 (-51.8)	147/241 (-50.7)	142/241 (-51.7)	137/241 (-51.1)	140/241 (-51.6)	137/241 (-52.5)	131/241 (-54.7)	132/241 (-55.2)
Pain										
UPA continued	288/397 (-49.0)	289/397 (-49.2)	289/397 (-48.0)	286/397 (-48.6)	281/397 (-48.7)	279/397 (-48.9)	280/397 (-47.6)	273/397 (-48.5)	271/397 (-48.8)	265/397 (-48.4)
ADA continued	112/168 (-42.6)	112/168 (-44.4)	111/168 (-46.8)	113/168 (-47.3)	109/168 (-46.7)	106/168 (-44.6)	105/168 (-47.8)	105/168 (-49.0)	99/168 (-46.8)	101/168 (-47.6)
PBO to UPA	445/648 (-44.2)	450/648 (-43.1)	441/648 (-44.4)	447/648 (-44.0)	440/648 (-42.8)	433/648 (-43.5)	437/648 (-43.3)	428/648 (-45.1)	419/648 (-43.6)	417/648 (-43.2)
ADA to UPA	115/157 (-44.8)	111/157 (-44.5)	109/157 (-45.8)	112/157 (-43.5)	109/157 (-43.8)	107/157 (-44.9)	107/157 (-43.6)	102/157 (-43.0)	101/157 (-41.8)	99/157 (-44.0)
UPA to ADA	164/250 (-39.0)	161/250 (-39.5)	156/250 (-40.3)	154/250 (-39.7)	147/250 (-41.1)	145/250 (-40.7)	148/250 (-37.3)	148/250 (-41.0)	139/250 (-41.0)	140/250 (-41.3)
HAQ-DI										
UPA continued	288/397 (-1.00)	289/397 (-1.00)	289/397 (-0.99)	286/397 (-1.01)	281/397 (-1.01)	279/397 (-0.98)	280/397 (-0.99)	273/397 (-1.00)	271/397 (-0.98)	265/397 (-0.98)
ADA continued	112/168 (-0.84)	112/168 (-0.83)	110/168 (-0.90)	113/168 (-0.85)	109/168 (-0.89)	106/168 (-0.80)	105/168 (-0.88)	105/168 (-0.91)	99/168 (-0.85)	101/168 (-0.88)
PBO to UPA	444/648 (-0.86)	448/648 (-0.86)	441/648 (-0.86)	447/648 (-0.86)	440/648 (-0.86)	433/648 (-0.87)	436/648 (-0.88)	428/648 (-0.87)	419/648 (-0.86)	417/648 (-0.86)
ADA to UPA	115/157	111/157	109/157	112/157	109/157	107/157	107/157	102/157	101/157	99/157

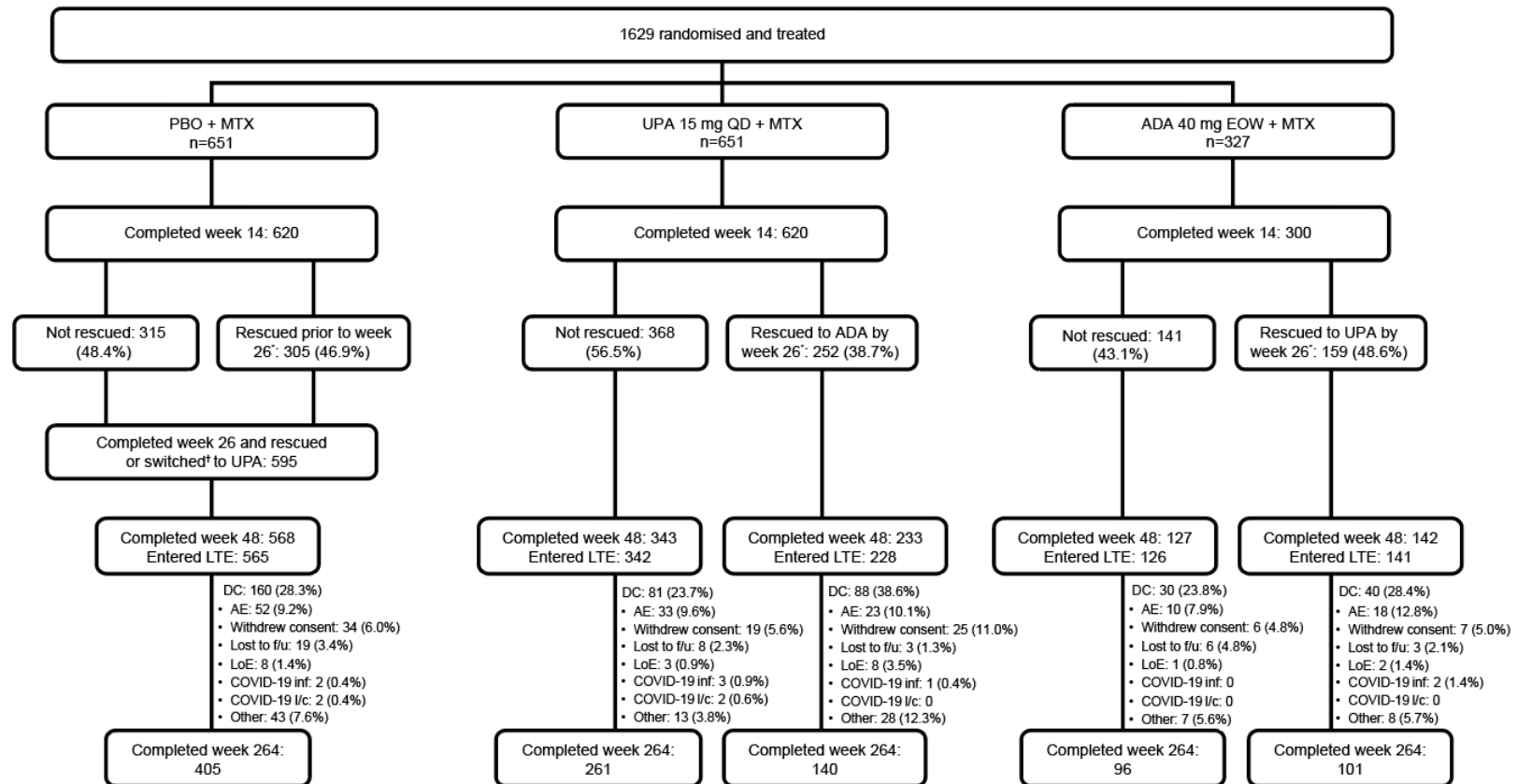
UPA to ADA	(-0.91) 163/249 (-0.75)	(-0.92) 160/249 (-0.70)	(-0.92) 155/249 (-0.77)	(-0.91) 153/249 (-0.73)	(-0.91) 146/249 (-0.74)	(-0.86) 144/249 (-0.75)	(-0.84) 147/249 (-0.70)	(-0.83) 147/249 (-0.76)	(-0.87) 138/249 (-0.75)	(-0.89) 138/249 (-0.78)
hsCRP										
UPA continued	268/399 (-14.1)	271/399 (-13.4)	262/399 (-13.8)	264/399 (-13.5)	262/399 (-12.7)	259/399 (-12.6)	269/399 (-11.9)	256/399 (-12.5)	257/399 (-13.1)	252/399 (-12.3)
ADA continued	101/167 (-9.5)	96/167 (-10.2)	96/167 (-9.8)	103/167 (-9.3)	98/167 (-9.7)	94/167 (-7.6)	92/167 (-7.3)	97/167 (-10.3)	90/167 (-8.2)	95/167 (-10.0)
PBO to UPA	406/650 (-14.9)	403/650 (-13.5)	405/650 (-14.0)	417/650 (-13.9)	410/650 (-13.5)	395/650 (-14.5)	414/650 (-13.7)	404/650 (-13.8)	389/650 (-12.7)	390/650 (-13.6)
ADA to UPA	107/159 (-18.4)	100/159 (-21.1)	95/159 (-19.5)	105/159 (-18.0)	102/159 (-16.5)	101/159 (-17.3)	102/159 (-17.1)	97/159 (-16.0)	94/159 (-13.1)	93/159 (-19.3)
UPA to ADA	153/252 (-12.0)	148/252 (-10.3)	145/252 (-13.3)	145/252 (-11.7)	137/252 (-12.5)	137/252 (-13.1)	140/252 (-9.7)	139/252 (-13.3)	134/252 (-12.3)	132/252 (-13.3)
ΔmTSS										
UPA continued	—	—	—	288 (0.53)	—	—	—	—	—	—
ADA continued	—	—	—	109 (1.18)	—	—	—	—	—	—
PBO to UPA	—	—	—	442 (1.27)	—	—	—	—	—	—
ADA to UPA	—	—	—	111 (0.88)	—	—	—	—	—	—
UPA to ADA	—	—	—	150 (1.72)	—	—	—	—	—	—
Severity of morning stiffness (0–10 NRS)										
UPA continued	297/399 (-5.2)	295/399 (-5.1)	291/399 (-5.1)	289/399 (-5.1)	285/399 (-5.0)	282/399 (-5.2)	283/399 (-5.1)	227/399 (-5.2)	275/399 (-5.1)	268/399 (-5.1)
ADA continued	114/167 (-4.6)	111/167 (-4.8)	111/167 (-4.8)	112/167 (-4.8)	108/167 (-4.6)	106/167 (-4.7)	105/167 (-4.8)	105/167 (-4.8)	101/167 (-4.9)	101/167 (-4.8)
PBO to UPA	456/650 (-4.8)	456/650 (-4.8)	451/650 (-4.9)	453/650 (-4.8)	444/650 (-4.8)	439/650 (-4.9)	440/650 (-4.8)	431/650 (-4.8)	425/650 (-4.9)	422/650 (-4.8)
ADA to UPA	116/157 (-4.8)	115/157 (-4.9)	110/157 (-4.8)	112/157 (-4.9)	110/157 (-4.7)	108/157 (-4.9)	107/157 (-4.8)	102/157 (-4.6)	101/157 (-4.7)	100/157 (-4.7)
UPA to ADA	162/249 (-4.0)	161/249 (-4.2)	156/249 (-4.2)	155/249 (-4.4)	147/249 (-4.2)	146/249 (-4.4)	146/249 (-4.3)	148/249 (-4.1)	142/249 (-4.3)	141/249 (-4.4)
Duration of morning stiffness (mins)										
UPA continued	297/399 (-132.8)	295/399 (-132.0)	292/399 (-134.4)	289/399 (-133.8)	285/399 (-132.6)	282/399 (-136.8)	283/399 (-133.1)	277/399 (-135.3)	275/399 (-135.1)	268/399 (-137.1)
ADA continued	114/167 (-98.6)	111/167 (-102.4)	111/167 (-102.6)	112/167 (-102.4)	108/167 (-83.3)	106/167 (-97.9)	105/167 (-91.8)	106/167 (-104.3)	101/167 (-103.4)	101/167 (-100.9)
PBO to UPA	456/650 (-131.3)	456/650 (-122.6)	451/650 (-131.2)	454/650 (-124.4)	444/650 (-128.6)	439/650 (-126.5)	441/650 (-125.5)	431/650 (-129.2)	425/650 (-122.8)	422/650 (-127.2)
ADA to UPA	116/157 (-152.7)	115/157 (-155.2)	110/157 (-148.5)	112/157 (-148.9)	110/157 (-150.5)	108/157 (-142.1)	107/157 (-141.5)	102/157 (-138.2)	101/157 (-135.4)	100/157 (-124.6)
UPA to ADA	164/250	162/250	157/250	156/250	148/250	145/250	147/250	149/250	143/250	142/250

(-109.9)	(-108.1)	(-99.3)	(-116.5)	(-110.7)	(-120.8)	(-117.4)	(-114.3)	(-117.2)	(-117.1)
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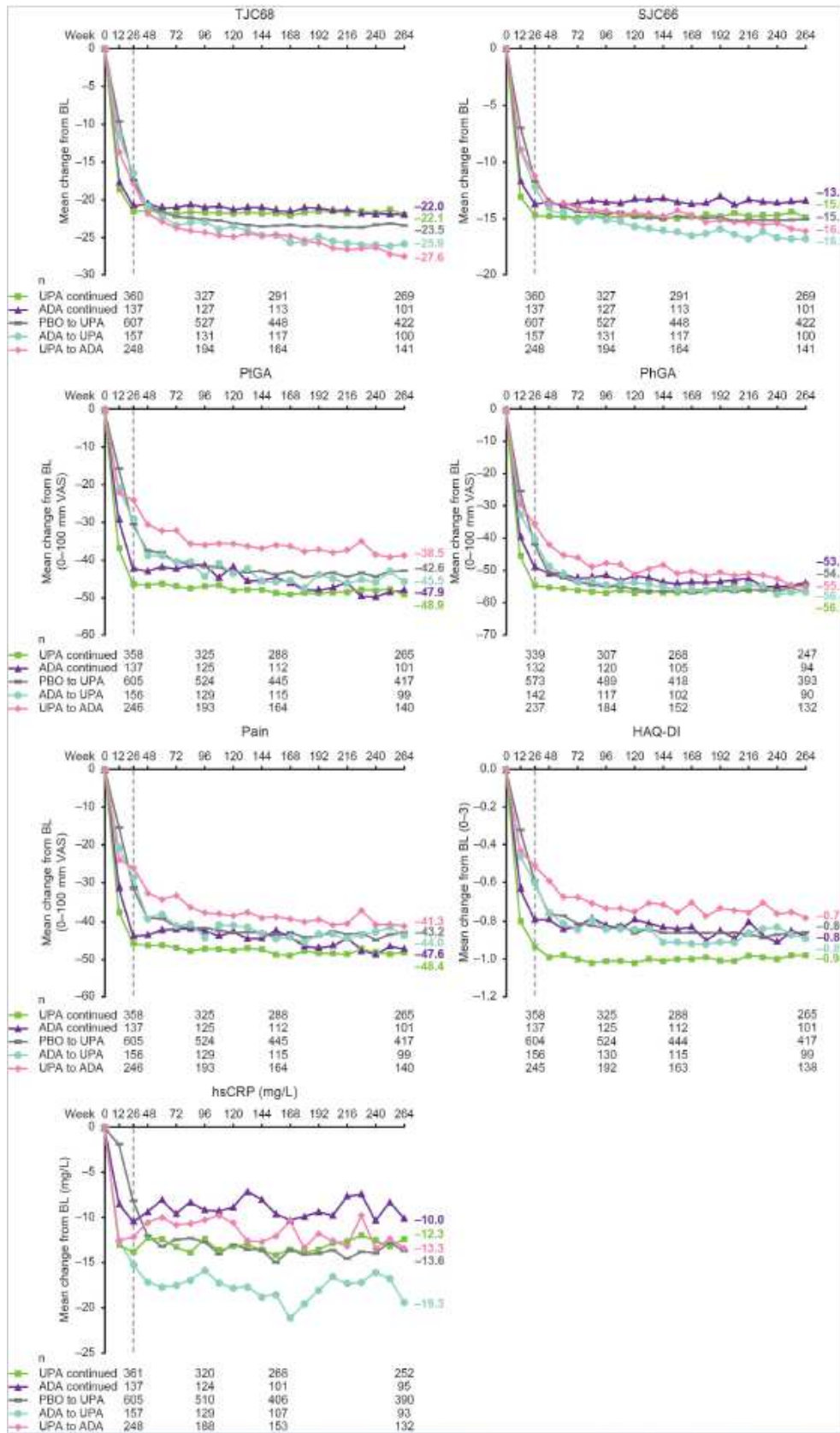
Categorical data points of categorical endpoints analysed by treatment sequence AO, without imputation for missing data shown in Figure 5 (radiographic outcomes), supplementary figure S3 (ACR components) and supplementary figure S4 (morning stiffness). Δ , change from baseline; ACR, American College of Rheumatology; ADA, adalimumab; AO, as observed; BL, baseline; HAQ-DI, Health Assessment Questionnaire – Disability Index; hsCRP, high-sensitivity C-reactive protein; mTSS, modified Total Sharp Score; NRS, numerical rating scale; PBO, placebo; PhGA, physician’s global assessment of disease activity; PtGA, patient’s global assessment of disease activity; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; UPA, upadacitinib.



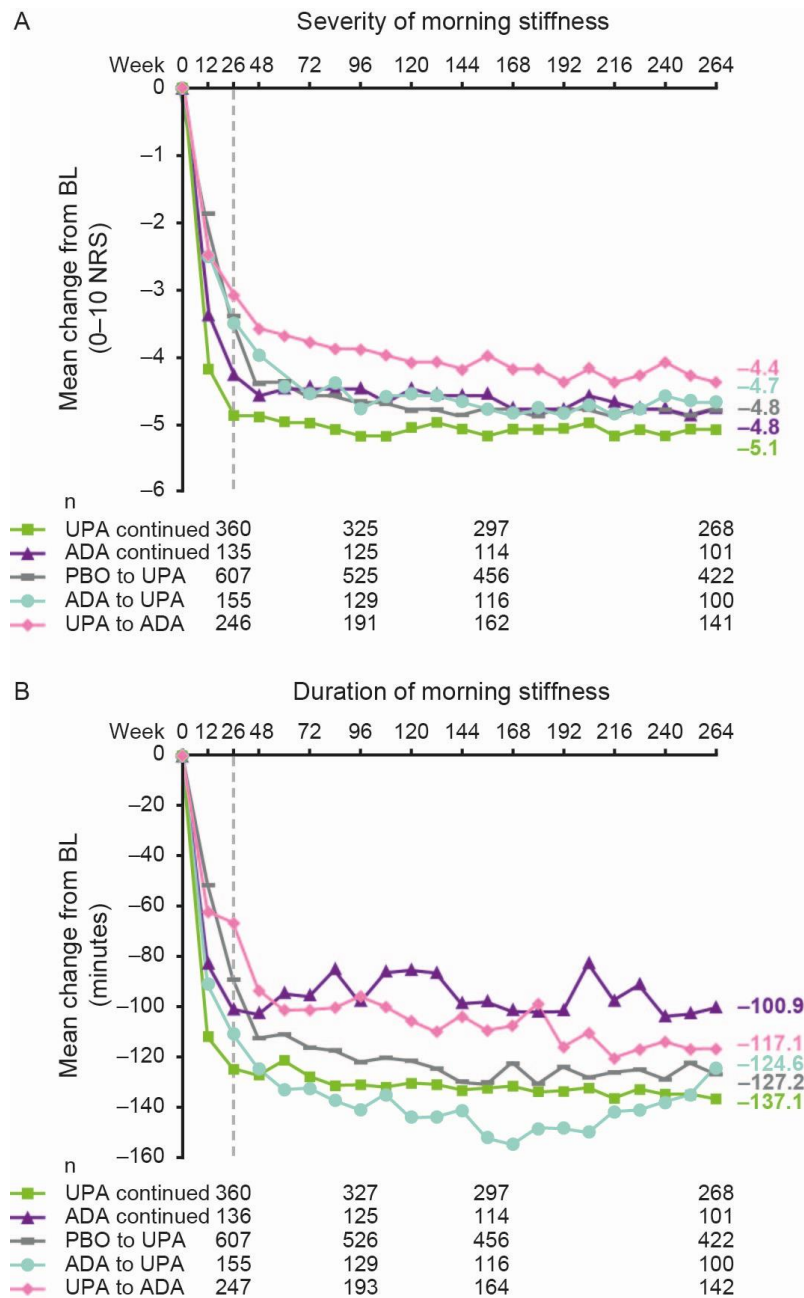
Supplementary Figure S1 SELECT-COMPARE study design. Patients continued treatment with UPA or ADA in a blinded manner until the last patient completed the week 48 visit; patients received open-label treatment of the study drug they were assigned to thereafter. *Primary endpoints at week 12: ACR20 (Food and Drug Administration) and DAS28(CRP) <2.6 (European Medicines Agency). †Rescue: at weeks 14, 18 and 22 if <20% improvement in TJC66 or SJC68 versus BL; at week 26 if CDAI >10. ACR20, ≥20% improvement in American College of Rheumatology response criteria; ADA, adalimumab; BL, baseline; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score based on C-reactive protein; EOW, every other week; LTE, long-term extension; MTX, methotrexate; PBO, placebo; QD, once daily; RA, rheumatoid arthritis; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; UPA, upadacitinib.



Supplementary Figure S2 Patient disposition through 264 weeks. Number of patients on study drug, with primary reason for discontinuation summarised during long-term extension through 264 weeks. *Rescue occurred only before or at week 26; no rescue was allowed after week 26. †All PBO patients not previously rescued (at weeks 14, 18 or 22) were switched to UPA at week 26. ADA, adalimumab; AE, adverse event; DC, discontinued; EOW, every other week; f/u, follow-up; inf, infection; l/c, logistical restrictions; LoE, lack of efficacy; LTE, long-term extension; MTX, methotrexate; PBO, placebo; QD, once daily; UPA, upadacitinib.

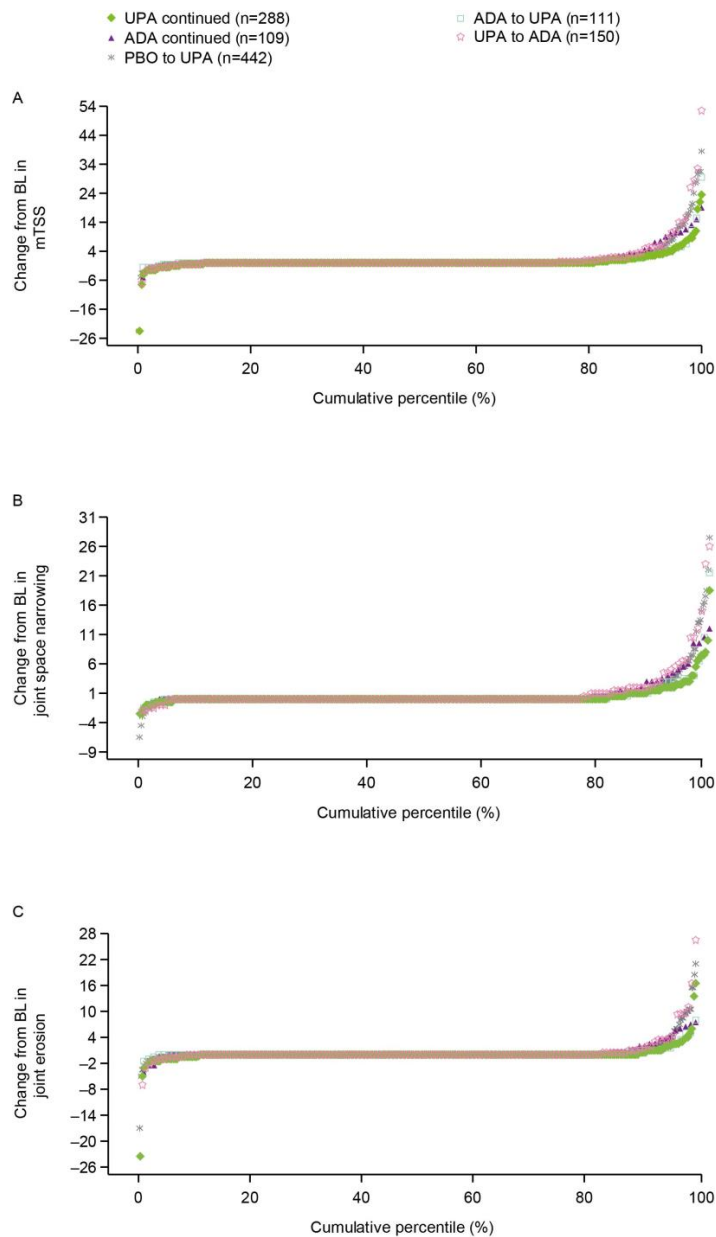


Supplementary Figure S3 Mean change from BL in core components of ACR criteria through 264 weeks (AO). Groups are by treatment sequence AO, without imputation for missing data. All patients in the PBO group who were not previously rescued were switched to UPA at week 26. Data points plotted here are shown in supplementary table S10. ACR, American College of Rheumatology; ADA, adalimumab; AO, as observed; BL, baseline; HAQ-DI, Health Assessment Questionnaire – Disability Index; hsCRP, high-sensitivity C-reactive protein; PBO, placebo; PhGA, physician’s global assessment of disease activity; PtGA, patient’s global assessment of disease activity; SJC66, swollen joint count based on 66 joints; TJC68, tender joint count based on 68 joints; UPA, upadacitinib; VAS, visual analogue scale.



Supplementary Figure S4 Mean change from baseline in severity and duration of morning stiffness

through 264 weeks (AO). Groups are by treatment sequence AO, without imputation for missing data. All patients in the PBO group who were not previously rescued were switched to UPA at week 26. Data points plotted here are shown in supplementary table S10. ADA, adalimumab; AO, as observed; BL, baseline; NRS, numerical rating scale; PBO, placebo; UPA, upadacitinib.



Supplementary Figure S5 Probability plots of change from baseline in mTSS, joint erosion and joint space narrowing at week 192 (AO). Groups are by treatment sequence AO, without imputation for missing data. All patients in the PBO group who were not previously rescued were switched to UPA at week 26. ADA, adalimumab; AO, as observed; BL, baseline; mTSS, modified Total Sharp Score; PBO, placebo; UPA, upadacitinib.