Supplementary file

Supplementary text on malignancies

Across all four treatment arms, a total of 32 malignancy events (15 with upadacitinib 30 mg QD, 10 with upadacitinib 15 mg QD, two with placebo/upadacitinib 30 mg QD, and five with placebo/upadacitinib 15 mg QD) were reported in 24 patients; nine were male and 15 were female, and the median age was 59 years (range, 28–75 years). Overall, 10 events were considered as serious, five events were considered by the investigator as having a reasonable possibility of being related to the study drug, and nine events resulted in discontinuation of the study drug. The median time to onset was 565 days (range, 64–1051 days), with a median of 540 days following the initiation of upadacitinib. At the end of the study, 10 events were ongoing.

Of note, two events of basal cell carcinoma in the same patient were diagnosed at the same assessment and were recorded as a single event in the overview data.

Supplementary Table S1. Key continuous efficacy endpoints at week 152 in patients with prior inadequate response to tumour necrosis factor inhibitors (MMRM† on as-observed data).

Parameter	UPA 15 mg QD		UPA 30 mg QD*		Placebo/upadacitinib 15 mg QD		Placebo/upadacitinib 30 mg QD*	
	n‡	LSM change from baseline (95% CI)	n‡	LSM change from baseline (95% CI)	n‡	LSM change from baseline (95% CI)	n‡	LSM change from baseline (95% CI)
HAQ-DI score	157	-0.4 (-0.5, -0.3)	173	-0.5 (-0.6, -0.4)	78	-0.5 (-0.7, -0.4)	83	-0.4 (-0.5, -0.2)
SF-36 PCS	156	7.4 (5.9, 8.9)	170	7.9 (6.4, 9.3)	72	6.8 (4.3, 9.3)	81	5.1 (2.9, 7.3)
SF-36 MCS	156	2.6 (0.9, 4.3)	170	3.4 (1.8, 5.1)	72	3.4 (0.6, 6.2)	81	3.7 (1.2, 6.1)
Pain (0–10 NRS)	157	-2.8 (-3.2, -2.4)	173	-2.5 (-2.9, -2.0)	78	-2.3 (-3.0, -1.6)	83	-2.5 (-3.1, -1.9)
BASDAI§	60	-2.5 (-3.1, -1.9)	56	-2.1 (-2.7, -1.4)	29	-2.6 (-3.6, -1.6)	30	-2.5 (-3.3, -1.6)
ASDAS§	60	-1.4 (-1.7, -1.1)	56	-1.2 (-1.4, -0.1)	29	-1.1 (-1.5, -0.6)	30	-1.3 (-1.6, -0.9)

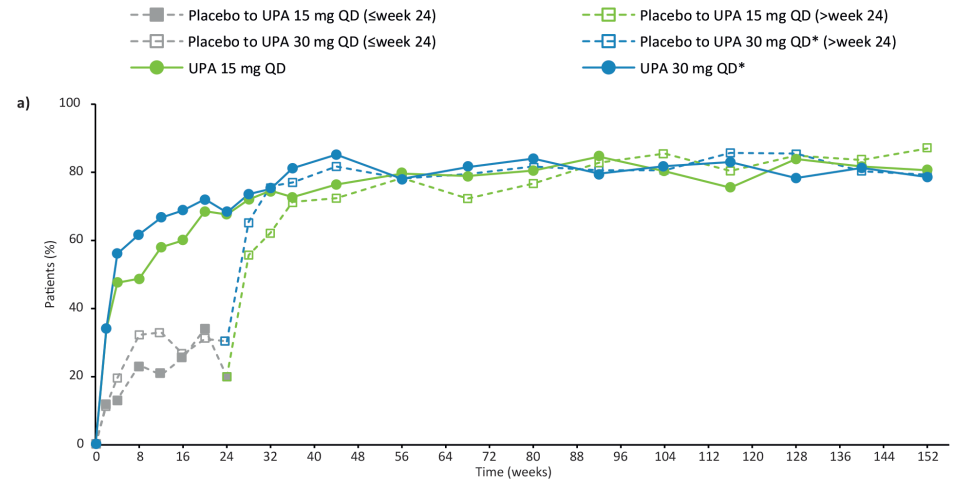
†MMRM analysis includes treatment, visit, treatment-by-visit interaction, and current DMARD use (yes/no) as fixed factors and baseline value as covariate. Patient's discontinuation status is also included in the model. Unstructured covariance structure is used. Data as observed at all visits are included in the model.

*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.

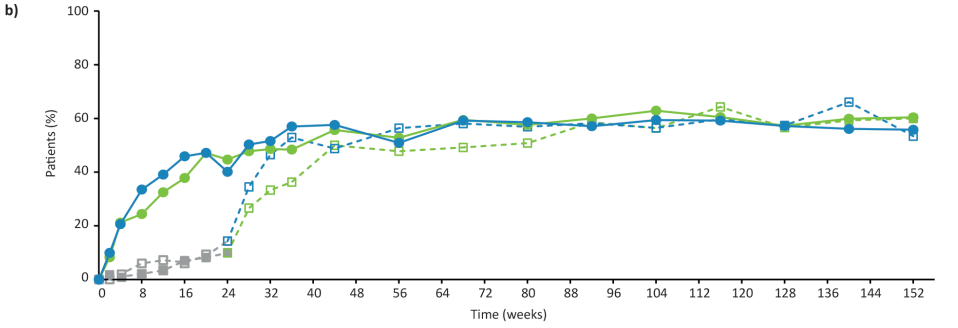
‡Number of unique patients contributing to MMRM estimates: patients with at least one available change from baseline value and no missing data for the factors and covariates in the model.

§Among patients with psoriatic spondylitis at baseline, as determined by investigator assessment.

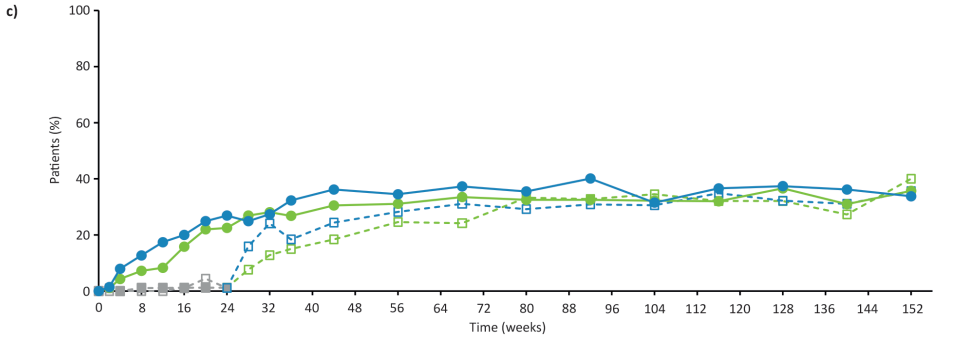
ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CI: confidence interval; DMARD: disease-modifying anti-rheumatic drug; HAQ-DI: Health Assessment Questionnaire – Disability Index; LSM: least squares mean; MCS: mental component summary; MMRM: mixed effect model for repeated measures; NRS: Numeric Rating Scale; PCS: physical component summary; QD: once daily; SF-36: 36-item Short-Form questionnaire; UPA: upadacitinib.



Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD																				
n	98	98	94	88	86	85	80	79	77	80	76	69	65	60	58	55	56	53	55	54
%	12.2	13.3	23.4	20.5	25.6	34.1	20.0	55.7	62.3	71.3	72.4	78.3	72.3	76.7	82.8	85.5	80.4	84.9	83.6	87.0
Placebo/UPA 30 mg QD*																				
n	103	102	99	97	94	90	92	87	87	87	82	78	73	71	67	62	63	62	61	58
%	11.7	19.6	32.3	33.0	26.6	31.1	30.4	65.5	75.9	77.0	81.7	78.2	79.5	81.7	80.6	80.6	85.7	85.5	80.3	79.3
UPA 15 mg QD																				
n	203	208	205	205	195	191	188	186	185	183	174	162	152	149	149	142	147	143	142	139
%	34.0	47.6	48.8	58.0	60.0	68.6	67.6	72.0	74.6	72.7	76.4	79.6	78.9	80.5	84.6	80.3	75.5	83.9	81.7	80.6
UPA 30 mg QD*																				
n	213	214	212	207	205	197	192	193	185	186	176	169	157	150	147	143	141	138	139	131
%	34.3	56.1	61.8	66.7	68.8	72.1	68.2	73.6	75.1	81.2	85.2	78.1	81.5	84.0	79.6	81.8	83.0	78.3	81.3	78.6

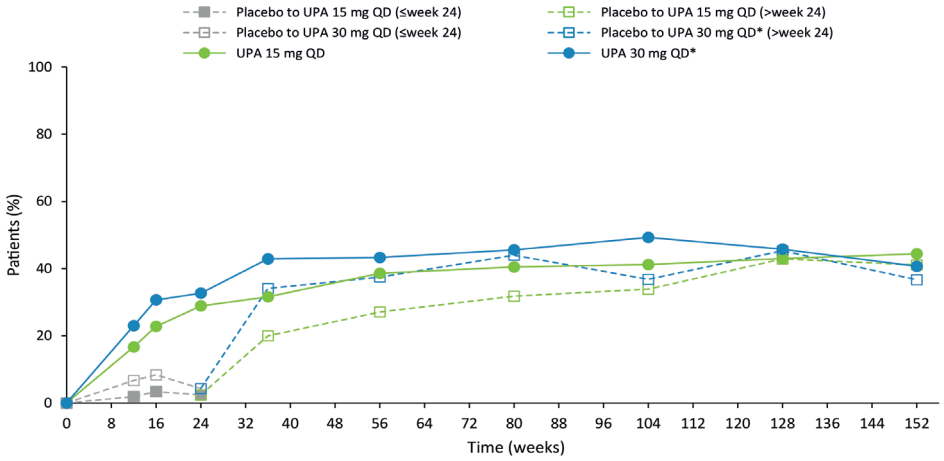


Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD																				
n	100	98	94	88	86	85	81	79	78	80	76	69	65	59	58	55	56	53	54	55
%	2.0	1.0	2.1	3.4	7.0	8.2	9.9	26.6	33.3	36.3	50.0	47.8	49.2	50.8	58.6	56.4	64.3	56.6	59.3	60.0
Placebo/UPA 30 mg QD*																				
n	104	103	100	97	94	91	91	87	86	87	82	78	74	72	67	62	62	61	62	58
%	0	1.9	6.0	7.2	6.4	8.8	14.3	34.5	46.5	52.9	48.8	56.4	58.1	56.9	58.2	56.5	59.7	57.4	66.1	53.4
UPA 15 mg QD																				
n	204	208	205	206	196	191	188	186	185	182	174	163	153	151	150	143	147	143	142	139
%	8.3	21.2	24.4	32.5	37.8	47.1	44.7	47.8	48.6	48.4	55.7	52.8	59.5	57.6	60.0	62.9	60.5	57.3	59.9	60.4
UPA 30 mg QD*																				
n	212	214	212	207	205	197	192	193	186	186	177	169	157	152	147	143	142	138	139	129
%	9.9	20.6	33.5	39.1	45.9	47.2	40.1	50.3	51.6	57.0	57.6	50.9	59.2	58.6	57.1	59.4	59.2	57.2	56.1	55.8



Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD																				
n	100	98	94	88	86	85	81	79	78	80	76	69	66	60	58	55	56	53	55	55
%	1.0	0.0	1.1	1.1	1.2	1.2	1.2	7.6	12.8	15.0	18.4	24.6	24.2	33.3	32.8	34.5	32.1	32.1	27.3	40.0
Placebo/UPA 30 mg QD*																				
n	104	104	101	98	95	91	92	88	87	87	82	78	74	72	68	62	63	59	61	59
%	0.0	0.0	0.0	0.0	1.1	4.4	1.1	15.9	24.1	18.4	24.4	28.2	31.1	29.2	30.9	30.6	34.9	32.2	31.1	35.6
UPA 15 mg QD																				
n	205	208	207	204	196	191	187	186	185	183	174	164	155	151	151	143	147	142	142	140
%	1.0	4.3	7.2	8.3	15.8	22.0	22.5	26.9	28.1	26.8	30.5	31.1	33.5	32.5	32.5	32.2	32.0	36.6	31.0	35.7
UPA 30 mg QD*																				
n	214	215	212	207	205	197	193	193	186	186	177	168	158	152	147	143	142	139	138	130
%	1.4	7.9	12.7	17.4	20.0	24.9	26.9	24.9	27.4	32.3	36.2	34.5	37.3	35.5	40.1	31.5	36.6	37.4	36.2	33.8

Supplementary Fig. S1. Proportion of patients achieving **a**) ACR20, **b**) ACR50, and **c**) ACR70 over 152 weeks (as-observed data).
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
ACR20/50/70: 20/50/70% improvement in American College of Rheumatology criteria; QD: once daily; UPA: upadacitinib.



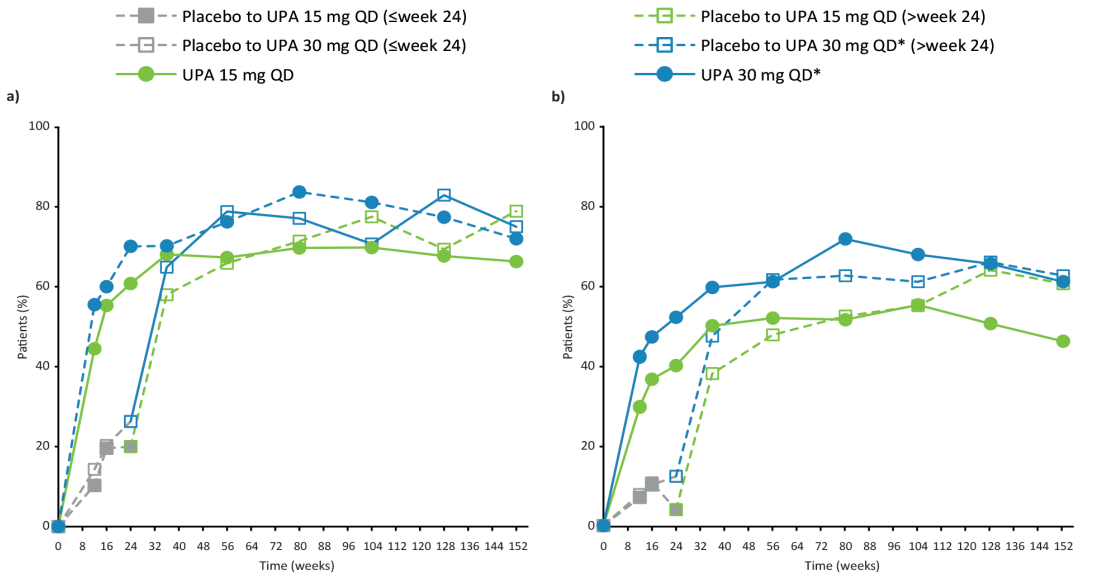
Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD									
n	102	87	83	80	70	66	59	56	56
%	2.0	3.4	2.4	20.0	27.1	31.8	33.9	42.9	41.1
Placebo/UPA 30 mg QD*									
n	105	95	92	91	80	75	68	64	60
%	6.7	8.4	4.3	34.1	37.5	44.0	36.8	45.3	36.7
UPA 15 mg QD									
n	210	197	194	187	166	163	153	149	144
%	16.7	22.8	28.9	31.6	38.6	40.5	41.2	43.0	44.4
UPA 30 mg QD*									
n	217	205	196	191	171	160	148	142	135
%	23.0	30.7	32.7	42.9	43.3	45.6	49.3	45.8	40.7

Supplementary Fig. S2. Proportion of patients achieving minimal disease activity over 152 weeks (as-observed data).
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit. QD: once daily; UPA: upadacitinib.

Supplementary Table S2. Treatment-emergent adverse events with a frequency of ≥5 events/100 PY in any treatment group.

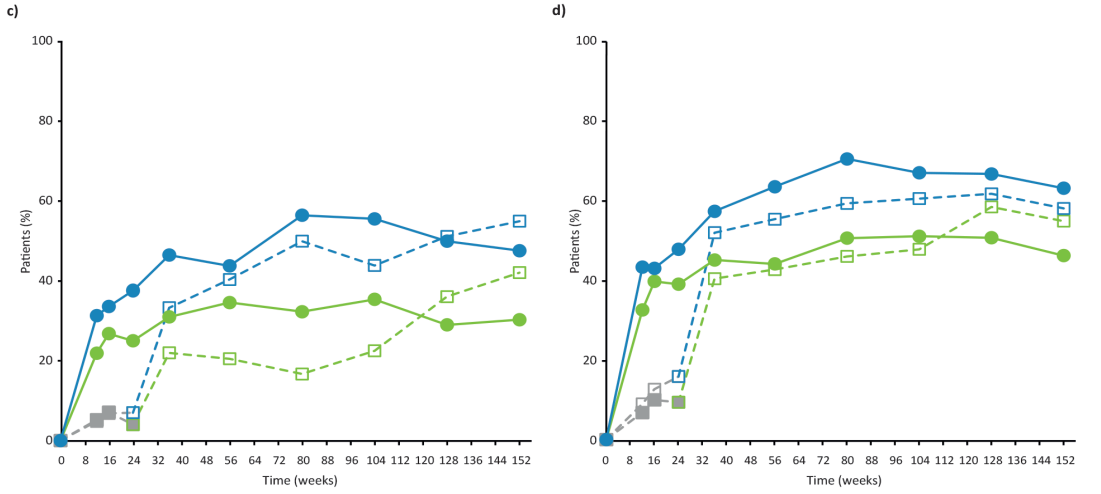
Adverse event	Upadacitinib 15 mg QD (n=290; 649.0 PY)		Upadacitinib 30 mg QD (n=308; 600.3 PY)		Upadacitinib 15 mg QD (switched from 30 mg QD) (n=87; 46.2 PY)	
	Events	Events per 100 PY	Events	Events per 100 PY	Events	Events per 100 PY
Urinary tract infection	57	8.8	51	8.5	2	4.3
Nasopharyngitis	56	8.6	59	9.8	2	4.3
Upper respiratory tract infection	49	7.6	53	8.8	1	2.2
Bronchitis	41	6.3	34	5.7	0	–
Hypertension	36	5.5	30	5.0	1	2.2
Psoriatic arthropathy	35	5.4	32	5.3	5	10.8
COVID-19	32	4.9	18	3.0	7	15.2
CPK elevation	30	4.6	48	8.0	2	4.3
Herpes zoster	22	3.4	37	6.2	0	–
Psoriasis	10	1.5	5	0.8	4	8.7
COVID-19 (asymptomatic)	0	–	1	0.2	4	8.7

CPK: creatine phosphokinase; PY: patient-years; QD: once daily



Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD									
n	58	56	50	50	44	42	40	36	38
%	10.3	19.6	20.0	58.0	65.9	71.4	77.5	69.4	78.9
Placebo/UPA 30 mg QD*									
n	63	59	57	57	52	48	41	41	40
%	14.3	20.3	26.3	64.9	78.8	77.1	70.7	82.9	75.0
UPA 15 mg QD									
n	128	123	120	116	104	99	96	93	89
%	44.5	55.3	60.8	68.1	67.3	69.7	69.8	67.7	66.3
UPA 30 mg QD*									
n	128	125	117	114	105	92	90	84	82
%	55.5	60.0	70.1	70.2	76.2	83.7	81.1	77.4	72.0

Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD									
n	58	56	50	50	44	42	40	36	38
%	6.9	10.7	4.0	38.0	47.7	52.4	55.0	63.9	60.5
Placebo/UPA 30 mg QD*									
n	63	59	57	57	52	48	41	41	40
%	7.9	10.2	12.3	47.4	61.5	62.5	61.0	65.9	62.5
UPA 15 mg QD									
n	128	123	120	116	104	99	96	93	89
%	29.7	36.6	40.0	50.0	51.9	51.5	55.2	50.5	46.1
UPA 30 mg QD*									
n	128	125	117	114	105	92	90	84	82
%	42.2	47.2	52.1	59.6	61.0	71.7	67.8	65.5	61.0



Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD									
n	58	56	50	50	44	42	40	36	38
%	5.2	7.1	4.0	22.0	20.5	16.7	22.5	36.1	42.1
Placebo/UPA 30 mg QD*									
n	63	59	57	57	52	48	41	41	40
%	4.8	6.8	7.0	33.3	40.4	50.0	43.9	51.2	55.0
UPA 15 mg QD									
n	128	123	120	116	104	99	96	93	89
%	21.9	26.8	25.0	31.0	34.6	32.3	35.4	29.0	30.3
UPA 30 mg QD*									
n	128	125	117	114	105	92	80	84	82
%	31.3	33.6	37.6	46.5	43.8	56.5	55.6	50.0	47.6

Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD									
n	74	70	64	64	56	52	50	46	49
%	6.8	10.0	9.4	40.6	42.9	46.2	48.0	58.7	55.1
Placebo/UPA 30 mg QD*									
n	78	71	69	69	63	57	51	50	48
%	9.0	12.7	15.9	52.2	55.6	59.6	60.8	62.0	58.3
UPA 15 mg QD									
n	168	158	153	150	131	124	115	114	112
%	32.7	39.9	39.2	45.3	44.3	50.8	51.3	50.9	46.4
UPA 30 mg QD*									
n	161	155	148	144	127	113	110	106	101
%	43.5	43.2	48.0	57.6	63.8	70.8	67.3	67.0	63.4

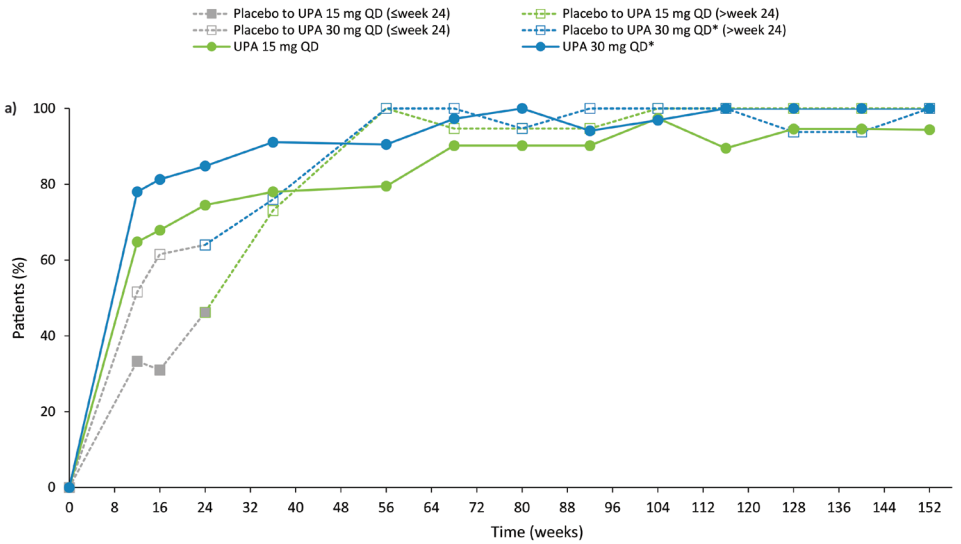
Supplementary Fig. S3. Proportion of patients achieving **a**) PASI 75†, **b**) PASI 90†, **c**) PASI 100†, and d) sIGA 0/1 and ≥2-point improvement from baseline over 152 weeks (as-observed data).

†PASI response rate assessed in patients with psoriasis body surface area ≥3% at baseline.

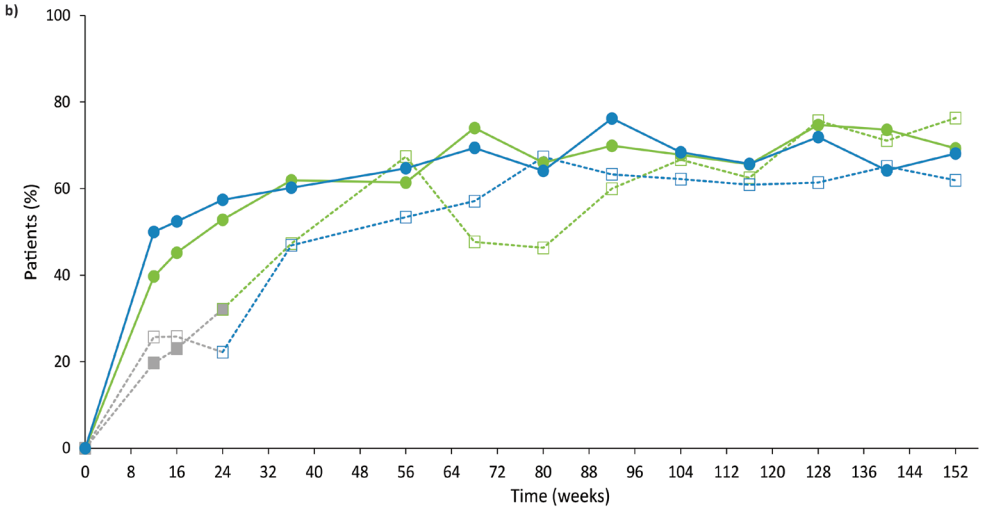
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.

PASI 75/90/100: 75/90/100% reduction in Psoriasis Area and Severity Index; QD: once daily; sIGA: static Investigator Global Assessment of Psoriasis; UPA: upadacitinib.

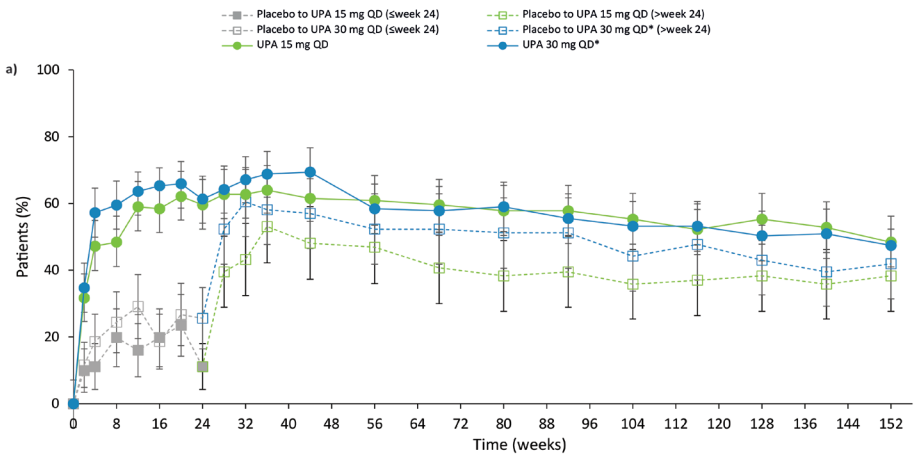
Supplementary Fig. S4. Proportion of patients achieving **a**) resolution of dactylitis (LDI = 0[†]) and **b**) resolution of enthesitis (LEI = 0[‡]) over 152 weeks (as-observed data).
[†]For patients with baseline LDI >0.
[‡]For patients with baseline LEI >0.
[*]All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; QD: once daily; UPA: upadacitinib.



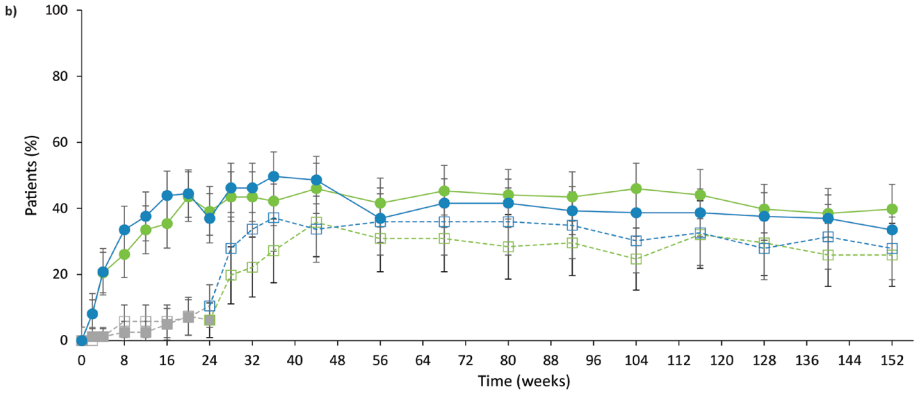
Week	12	16	24	36	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD													
n	30	29	26	26	20	19	19	19	18	18	18	17	18
%	33.3	31.0	46.2	73.1	100	94.7	94.7	94.7	100	100	100	100	100
Placebo/UPA 30 mg QD*													
n	31	26	25	25	23	21	19	18	17	17	16	16	16
%	51.6	61.5	64.0	76.0	100	100	94.7	100	100	100	93.8	93.8	100
UPA 15 mg QD													
n	54	53	51	50	44	41	41	41	38	38	37	37	36
%	64.8	67.9	74.5	78.0	79.5	90.2	90.2	90.2	97.4	89.5	94.6	94.6	94.4
UPA 30 mg QD*													
n	50	48	46	45	42	37	35	34	32	33	32	32	29
%	78.0	81.3	84.8	91.1	90.5	97.3	100	94.1	96.9	100	100	100	100



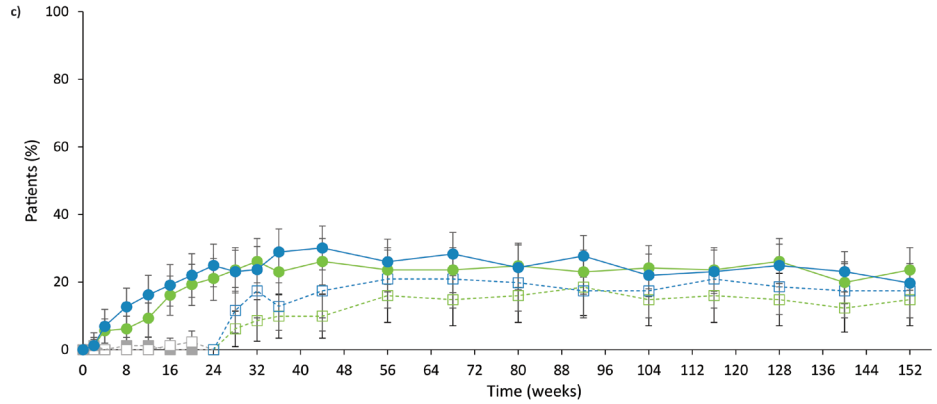
Week	12	16	24	36	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD													
n	66	61	56	55	46	44	41	40	39	40	37	38	38
%	19.7	23.0	32.1	47.3	67.4	47.7	46.3	60.0	66.7	62.5	75.7	71.1	76.3
Placebo/UPA 30 mg QD*													
n	70	66	63	64	58	56	52	49	45	46	44	43	42
%	25.7	25.8	22.2	46.9	53.4	57.1	67.3	63.3	62.2	60.9	61.4	65.1	61.9
UPA 15 mg QD													
n	131	124	123	118	101	96	94	93	90	93	91	91	88
%	39.7	45.2	52.8	61.9	61.4	74.0	66.0	69.9	67.8	65.6	74.7	73.6	69.3
UPA 30 mg QD*													
n	148	143	136	133	119	108	103	101	98	99	96	95	91
%	50.0	52.4	57.4	60.2	64.7	69.4	64.1	76.2	68.4	65.7	71.9	64.2	68.1



Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD (n=81)																				
%	9.9	11.1	19.8	16.0	19.8	23.5	11.1	39.5	43.2	53.1	48.1	46.9	40.7	38.3	39.5	35.8	37.0	38.3	35.8	38.3
Placebo/UPA 30 mg QD* (n=86)																				
%	11.6	18.6	24.4	29.1	18.6	26.7	25.6	52.3	60.5	58.1	57.0	52.3	52.3	51.2	51.2	44.2	47.7	43.0	39.5	41.9
UPA 15 mg QD (n=161)																				
%	31.7	47.2	48.4	59.0	58.4	62.1	59.6	62.7	62.7	64.0	61.5	60.9	59.6	57.8	57.8	55.3	52.2	55.3	52.8	48.4
UPA 30 mg QD* (n=173)																				
%	34.7	57.2	59.5	63.6	65.3	65.9	61.3	64.2	67.1	68.8	69.4	58.4	57.8	59.0	55.5	53.2	53.2	50.3	50.9	47.4



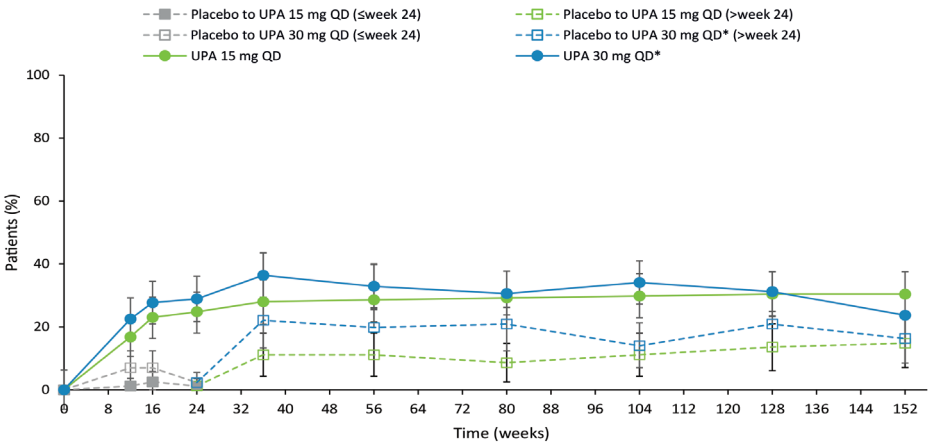
Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD (n=81)																				
%	1.2	1.2	2.5	2.5	4.9	7.4	6.2	19.8	22.2	27.2	35.8	30.9	30.9	28.4	29.6	24.7	32.1	29.6	25.9	25.9
Placebo/UPA 30 mg QD* (n=86)																				
%	0	1.2	5.8	5.8	5.8	7.0	10.5	27.9	33.7	37.2	33.7	36.0	36.0	36.0	34.9	30.2	32.6	27.9	31.4	27.9
UPA 15 mg QD (n=161)																				
%	8.1	20.5	26.1	33.5	35.4	43.5	39.1	43.5	43.5	42.2	46.0	41.6	45.3	44.1	43.5	46.0	44.1	39.8	38.5	39.8
UPA 30 mg QD* (n=173)																				
%	8.1	20.8	33.5	37.6	43.9	44.5	37.0	46.2	46.2	49.7	48.6	37.0	41.6	41.6	39.3	38.7	38.7	37.6	37.0	33.5



Week	2	4	8	12	16	20	24	28	32	36	44	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD (n=81)																				
%	1.2	0	1.2	1.2	0	0	0	6.2	8.6	9.9	9.9	16.0	14.8	16.0	18.5	14.8	16.0	14.8	12.3	14.8
Placebo/UPA 30 mg QD* (n=86)																				
%	0	0	0	0	1.2	2.3	0	11.6	17.4	12.8	17.4	20.9	20.9	19.8	17.4	17.4	20.9	18.6	17.4	17.4
UPA 15 mg QD (n=161)																				
%	1.2	5.6	6.2	9.3	16.1	19.3	21.1	23.6	26.1	23.0	26.1	23.6	23.6	24.8	23.0	24.2	23.6	26.1	19.9	23.6
UPA 30 mg QD* (n=173)																				
%	1.2	6.9	12.7	16.2	19.1	22.0	24.9	23.1	23.7	28.9	30.1	26.0	28.3	24.3	27.7	22.0	23.1	24.9	23.1	19.7

Supplementary Fig. S5. Proportion of patients with a prior inadequate response to tumour necrosis factor inhibitors achieving **a**) ACR20, **b**) ACR50, and **c**) ACR70 over 152 weeks (NRI). *All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
ACR20/50/70: 20/50/70% improvement in American College of Rheumatology criteria; NRI: non-responder imputation; QD: once daily; UPA: upadacitinib.

Supplementary Fig. S6. Proportion of patients with a prior inadequate response to tumour necrosis factor inhibitors achieving minimal disease activity over 152 weeks (NRI).
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
NRI: non-responder imputation;
QD: once daily; UPA: upadacitinib.

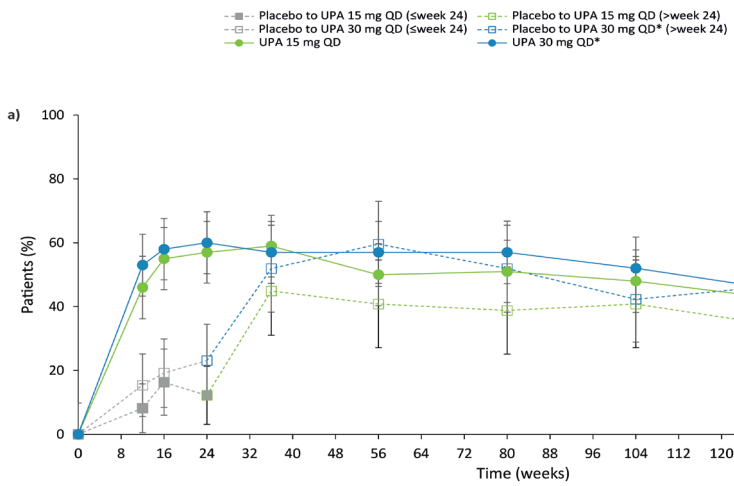


Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD (n=106)									
%	1.2	2.5	1.2	11.1	11.1	8.6	11.1	13.6	14.8
Placebo/UPA 30 mg QD* (n=106)									
%	7.0	7.0	2.3	22.1	19.8	20.9	14.0	20.9	16.3
UPA 15 mg QD (n=211)									
%	16.8	23.0	24.8	28.0	28.6	29.2	29.8	30.4	30.4
UPA 30 mg QD* (n=218)									
%	22.5	27.7	28.9	36.4	32.9	30.6	34.1	31.2	23.7

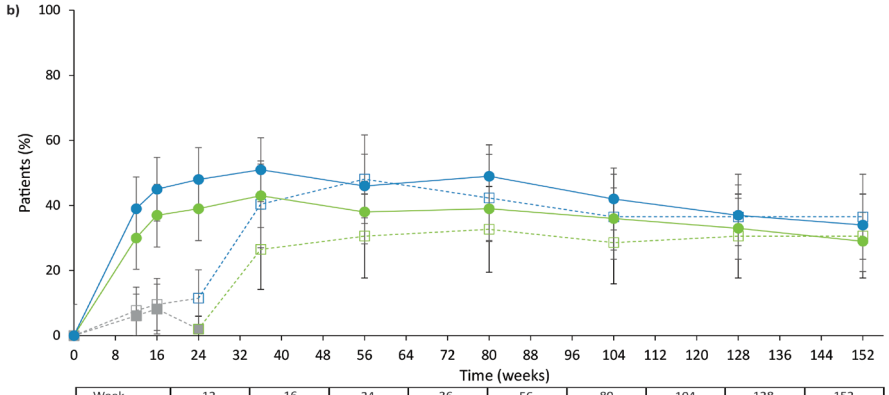
Supplementary Table S3. Treatment-emergent adverse events in patients who switched from upadacitinib 30 to 15 mg QD.

Adverse event	Upadacitinib 30/15 mg QD* (n=87; 46.2 PY)	
	Events	Events/100 PY (95% CI)
Any AE	72	155.8 (123.7, 196.3)
Any serious AE	4	8.7 (3.3, 23.1)
Any AE leading to discontinuation	2	4.3 (1.1, 17.3)
Any AE related to study drug†	11	23.8 (13.2, 43.0)
Any AE leading to death	0	0
Any COVID-19-related AE	11	23.8 (13.2, 43.0)
Infection	31	67.1 (47.2, 95.4)
Serious infection	3	6.5 (2.1, 20.1)
Opportunistic infection§	0	0
Herpes zoster	0	0
Active tuberculosis	0	0
Gastrointestinal perforation (adjudicated)	0	0
Hepatic disorder	0	0
Anaemia	0	0
Neutropenia	0	0
Lymphopenia	0	0
Creatine phosphokinase elevation	2	4.3 (1.1, 17.3)
Renal dysfunction	0	0
Any malignancy	1	2.2 (0.3, 15.4)
NMSC	0	0
Malignancy other than NMSC‡	1	2.2 (0.3, 15.4)
Lymphoma	0	0
Major adverse cardiovascular events (adjudicated)	0	0
Venous thromboembolic events (adjudicated)	0	0

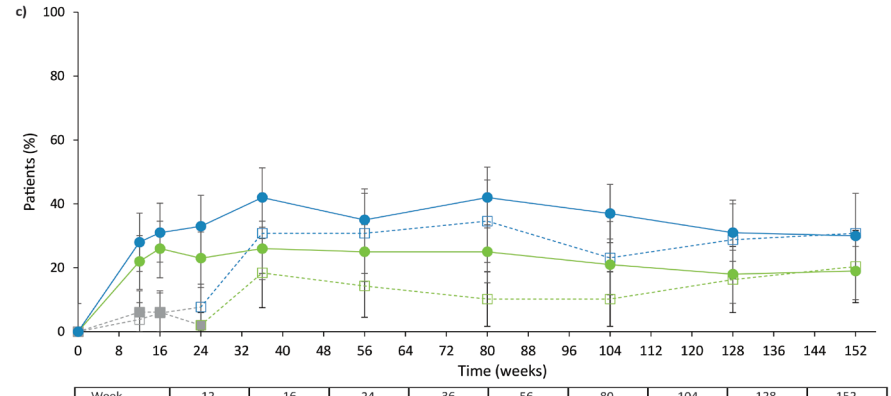
*Following a protocol amendment, all patients receiving upadacitinib 30 mg QD in the open-label extension were switched to the approved dose of 15 mg QD. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
†AEs with a reasonable possibility of being related to the study drug, in the opinion of the investigator.
§Excluding tuberculosis and herpes zoster. ‡One case of prostate cancer.
AE: adverse event; CI: confidence interval; NMSC: non-melanoma skin cancer; PY: patient-years; QD: once daily; SAE: serious adverse event.



Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD (n=49)									
%	8.2	16.3	12.2	44.9	40.8	38.8	40.8	34.7	38.8
Placebo/UPA 30 mg QD* (n=52)									
%	15.4	19.2	23.1	51.9	59.6	51.9	42.3	46.2	40.4
UPA 15 mg QD (n=100)									
%	46.0	55.0	57.0	59.0	50.0	51.0	48.0	43.0	42.0
UPA 30 mg QD* (n=100)									
%	53.0	58.0	60.0	57.0	57.0	57.0	52.0	46.0	40.0



Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD (n=49)									
%	6.1	8.2	2.0	26.5	30.6	32.7	28.6	30.6	30.6
Placebo/UPA 30 mg QD* (n=52)									
%	7.7	9.6	11.5	40.4	48.1	42.3	36.5	36.5	36.5
UPA 15 mg QD (n=100)									
%	30.0	37.0	39.0	43.0	38.0	39.0	36.0	33.0	29.0
UPA 30 mg QD* (n=100)									
%	39.0	45.0	48.0	51.0	46.0	49.0	42.0	37.0	34.0

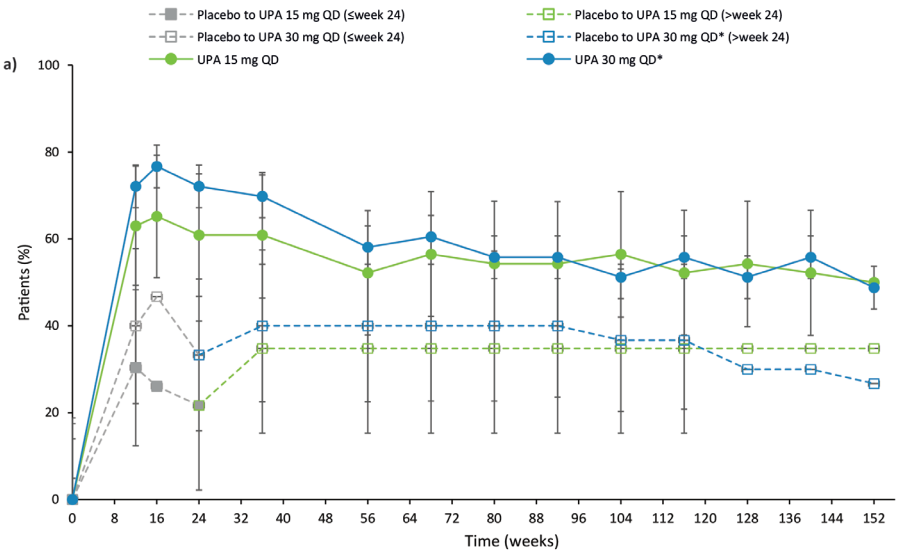


Week	12	16	24	36	56	80	104	128	152
Placebo/UPA 15 mg QD (n=49)									
%	6.1	6.1	2.0	18.4	14.3	10.2	10.2	16.3	20.4
Placebo/UPA 30 mg QD* (n=52)									
%	3.8	5.8	7.7	30.8	30.8	34.6	23.1	28.8	30.8
UPA 15 mg QD (n=100)									
%	22.0	26.0	23.0	26.0	25.0	25.0	21.0	18.0	19.0
UPA 30 mg QD* (n=100)									
%	28.0	31.0	33.0	42.0	35.0	42.0	37.0	31.0	30.0

Supplementary Fig. S7. Proportion of patients with a prior inadequate response to tumour necrosis factor inhibitors achieving **a**) PASI 75†, **b**) PASI 90†, and **c**) PASI 100† over 152 weeks (NRI).
†PASI response rate assessed in patients with psoriasis body surface area ≥3% at baseline.
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
NRI: non-responder imputation; PASI 75/90/100: 75/90/100% reduction in Psoriasis Area and Severity Index; QD: once daily; UPA: upadacitinib.

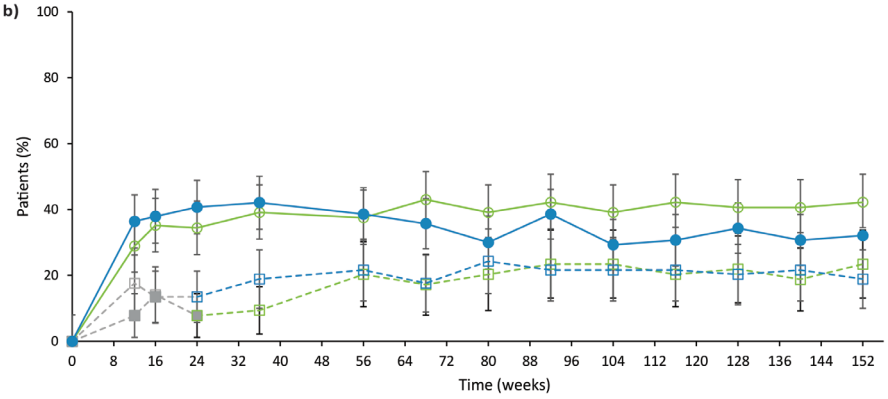
Supplementary Fig. S8. Proportion of patients with a prior inadequate response to tumour necrosis factor inhibitors achieving a) resolution of dactylitis (LDI =0†) and b) resolution of enthesitis (LEI =0‡) over 152 weeks (NRI).
†For patients with baseline LDI >0.
‡For patients with baseline LEI >0.
*All patients receiving UPA 30 mg QD were switched to UPA 15 mg QD during the open-label extension. The switch occurred at different visits across patients, with the earliest switch occurring at the week 116 visit.
LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; QD: once daily; UPA: upadacitinib.

a)

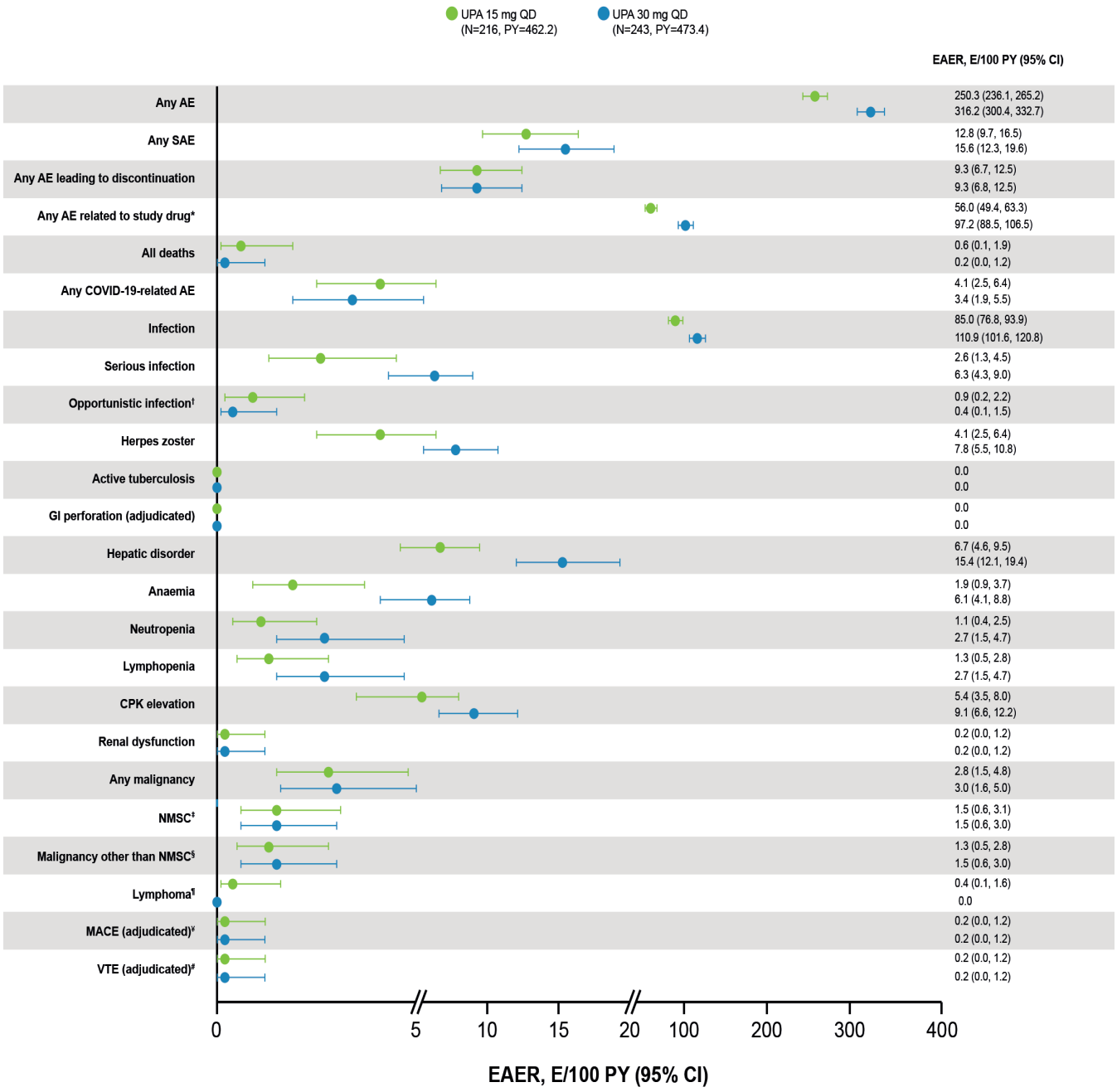


Week	12	16	24	36	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD (n=23)													
%	30.4	26.1	21.7	34.8	34.8	34.8	34.8	34.8	34.8	34.8	34.8	34.8	34.8
Placebo/UPA 30 mg QD* (n=30)													
%	40.0	46.7	33.3	40.0	40.0	40.0	40.0	40.0	36.7	36.7	30.0	30.0	26.7
UPA 15 mg QD (n=46)													
%	63.0	65.2	60.9	60.9	52.2	56.5	54.3	54.3	56.5	52.2	54.3	52.2	50.0
UPA 30 mg QD* (n=43)													
%	72.1	76.7	72.1	69.8	58.1	60.5	55.8	55.8	51.2	55.8	51.2	55.8	48.8

b)



Week	12	16	24	36	56	68	80	92	104	116	128	140	152
Placebo/UPA 15 mg QD (n=64)													
%	7.8	14.1	7.8	9.4	20.3	17.2	20.3	23.4	23.4	20.3	21.9	18.8	23.4
Placebo/UPA 30 mg QD* (n=74)													
%	17.6	13.5	13.5	18.9	21.6	17.6	24.3	21.6	21.6	21.6	20.3	21.6	18.9
UPA 15 mg QD (n=128)													
%	28.9	35.2	34.4	39.1	37.5	43.0	39.1	42.2	39.1	42.2	40.6	40.6	42.2
UPA 30 mg QD* (n=140)													
%	36.4	37.9	40.7	42.1	38.6	35.7	30.0	38.6	29.3	30.7	34.3	30.7	32.1



Supplementary Fig. S9. Treatment-emergent AEs in patients with a prior inadequate response to tumour necrosis factor inhibitors treated with UPA 15 or 30 mg.
*AEs with a reasonable possibility of being related to the study drug, in the opinion of the investigator.
†Excluding tuberculosis and herpes zoster.
‡Four cases of basal cell carcinoma and three cases of squamous cell carcinoma in the UPA 15 mg QD group (including one patient who had one event of basal cell carcinoma and two events of squamous cell carcinoma); three cases of basal cell carcinoma and four cases of squamous cell carcinoma in the UPA 30 mg QD group (including one patient who had two events of basal cell carcinoma and three events of squamous cell carcinoma).
§Two cases of prostate cancer and one case each of malignant melanoma (stage III), malignant neoplasm (not specified), ovarian cancer, and rectal cancer in the UPA 15 mg QD group; one case each of basosquamous carcinoma, endometrial cancer, intraductal papillary breast neoplasm, malignant melanoma, oropharyngeal squamous cell carcinoma, ovarian cancer, and rectal adenocarcinoma in the UPA 30 mg group (including one patient with both ovarian and endometrial cancer).
¶Two cases of abnormal lymphocyte morphology in the UPA 15 mg QD group are shown as this preferred term is included in the Malignant Lymphoma Standardised MedDRA Queries. These non-SAEs were based on single laboratory results and were not confirmed to be lymphomas.
¥Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
#Includes deep vein thrombosis and pulmonary embolism.
AE: adverse event; CPK: creatine phosphokinase; GI: gastrointestinal; MACE: major adverse cardiovascular events; MedDRA: Medical Dictionary for Regulatory Activities; NMSC: non-melanoma skin cancer; PY: patient-years; QD: once daily; SAE: serious adverse event; UPA: upadacitinib; VTE: venous thromboembolic events.