

Impact of Upadacitinib on Laboratory Parameters and Related Adverse Events in Patients with RA: Integrated Data Up to 6.5 Years

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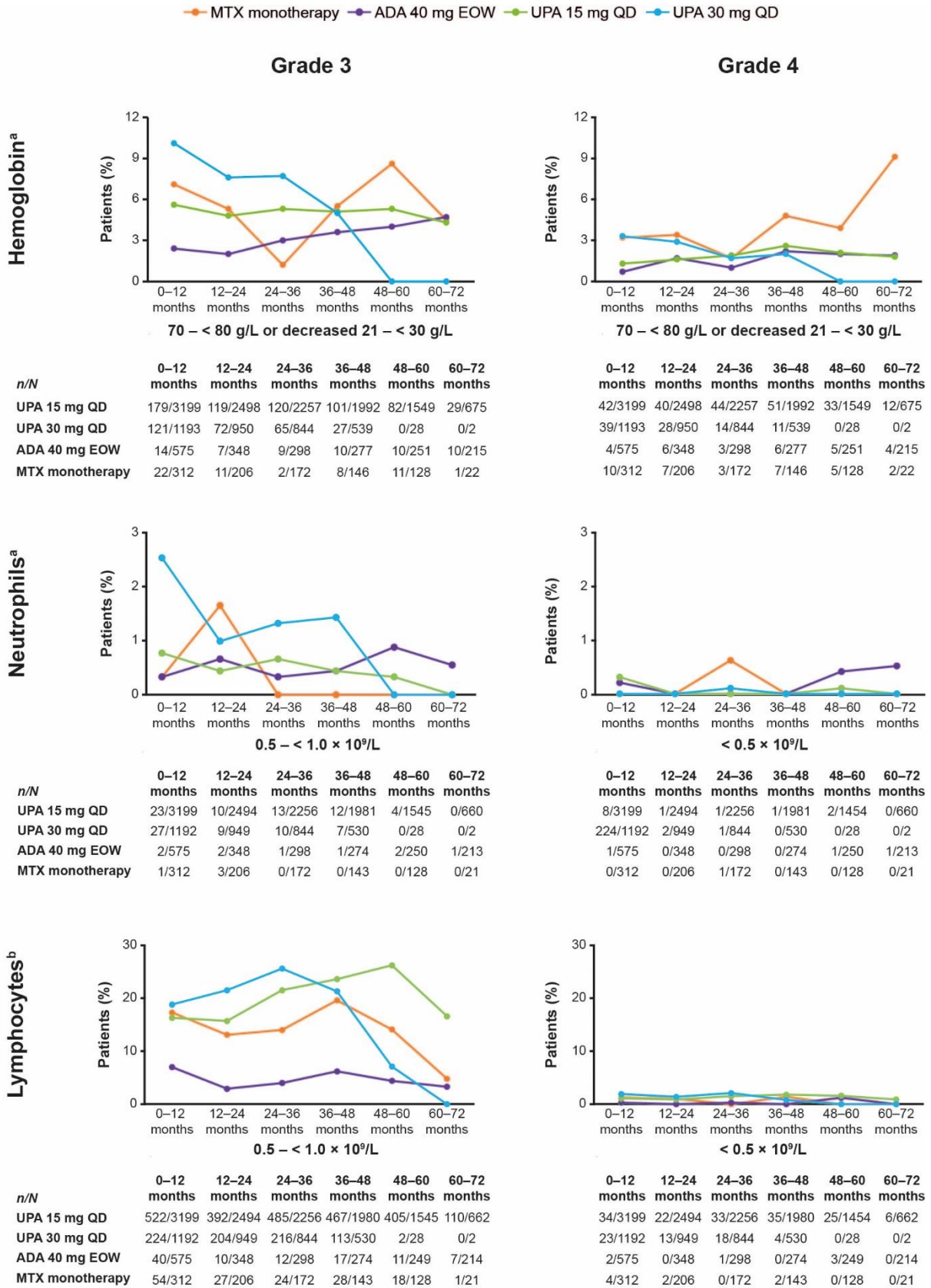
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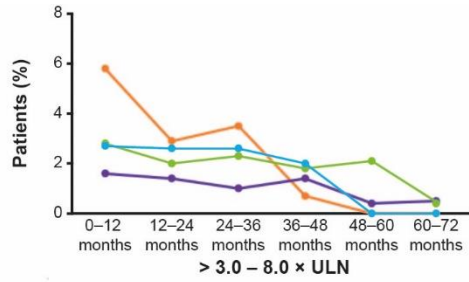
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ONLINE SUPPLEMENTARY APPENDIX

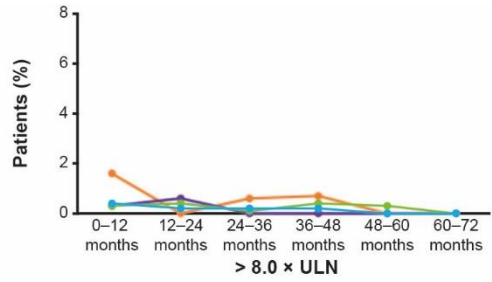
Supplementary Fig. S1. Patients with Grade 3 and 4 changes in laboratory parameters by 12-month time intervals, respectively



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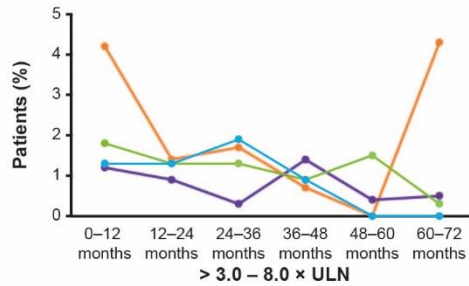


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	88/3197	49/2497	53/2257	35/1988	33/1551	3/662
UPA 30 mg QD	32/1195	25/955	22/848	11/543	0/28	0/2
ADA 40 mg EOW	9/576	5/350	3/298	4/277	1/250	1/217
MTX monotherapy	18/312	6/207	6/172	1/146	0/128	0/23

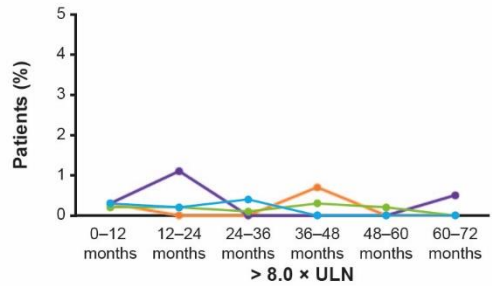


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	10/3197	11/2497	3/2257	7/1988	5/1551	0/682
UPA 30 mg QD	5/1195	2/955	2/848	1/543	0/28	0/2
ADA 40 mg EOW	2/576	2/350	0/298	0/277	0/250	0/217
MTX monotherapy	5/312	0/207	1/172	1/146	0/128	0/23

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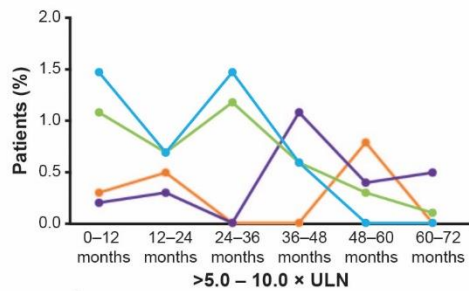


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	57/3197	32/2495	26/2257	17/1987	23/1551	2/690
UPA 30 mg QD	15/1196	12/955	13/847	5/541	0/26	0/2
ADA 40 mg EOW	7/576	3/350	0/298	4/277	1/250	1/218
MTX monotherapy	13/312	1/206	3/172	1/146	0/128	1/23

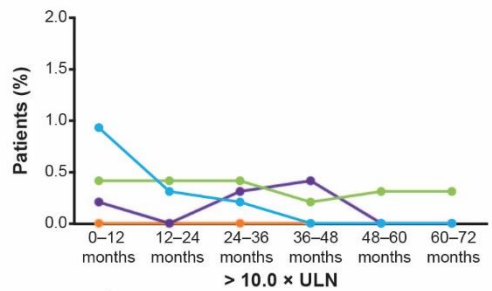


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	7/3197	6/2495	3/2257	6/1987	3/1551	0/690
UPA 30 mg QD	4/1995	2/955	3/848	0/541	0/26	0/2
ADA 40 mg EOW	2/576	4/350	0/298	0/277	0/250	1/218
MTX monotherapy	1/312	0/207	0/172	1/146	0/128	0/23

CPK^b

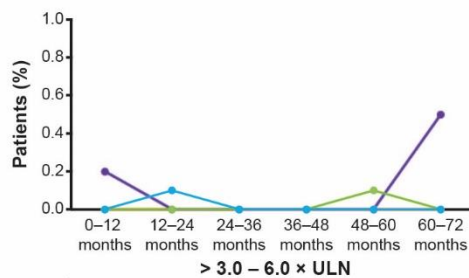


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	36/3197	18/2493	26/2257	11/1892	5/1456	1/683
UPA 30 mg QD	18/1196	7/955	13/847	3/533	0/27	0/2
ADA 40 mg EOW	1/576	1/347	0/298	3/277	1/250	1/216
MTX monotherapy	1/312	1/206	0/172	0/145	1/128	0/23

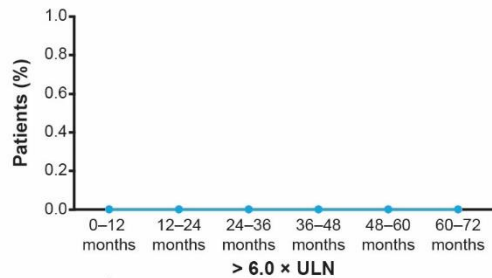


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	12/3197	10/2493	10/2257	3/1982	5/1546	2/683
UPA 30 mg QD	11/1966	3/955	2/847	0/533	0/27	0/2
ADA 40 mg EOW	1/576	0/347	1/298	1/277	0/250	0/216
MTX monotherapy	0/312	0/206	0/172	0/145	0/128	0/22

Creatinine^b



n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	1/3197	1/2499	0/2257	0/1989	2/1551	0/691
UPA 30 mg QD	1/1197	1/956	0/848	0/543	0/27	0/2
ADA 40 mg EOW	1/576	0/349	0/298	0/277	0/250	1/218
MTX monotherapy	0/312	0/206	0/172	0/146	0/128	0/23

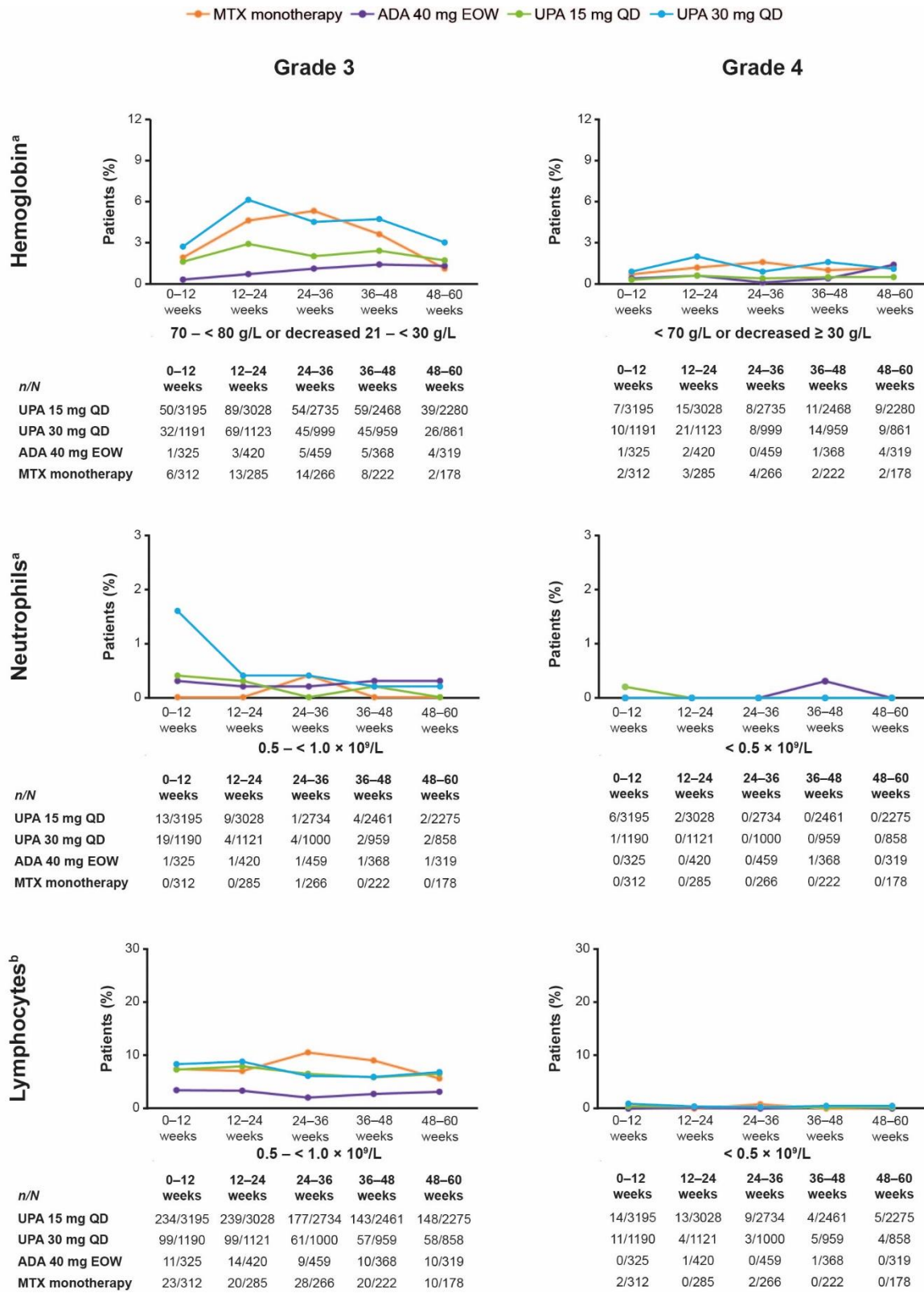


n/N	0-12 months	12-24 months	24-36 months	36-48 months	48-60 months	60-72 months
UPA 15 mg QD	1/3197	2/2499	1/2257	1/1989	1/1551	0/691
UPA 30 mg QD	0/1197	0/956	0/848	0/543	0/27	0/2
ADA 40 mg EOW	0/576	0/349	0/298	0/277	0/250	0/218
MTX monotherapy	0/312	0/206	0/172	0/146	0/128	0/23

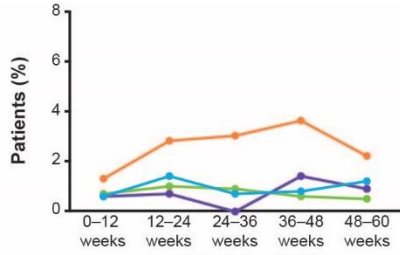
^aToxicity grading scale is based on OMERACT criteria. Post-baseline Grade must be higher than baseline Grade. ^bNational Cancer Institute standard common terminology criteria grading methodology was used. Post-baseline Grade must be higher than baseline Grade

ACPA anti-cyclic citrullinated protein antibody, *ADA* adalimumab, *BMI* body mass index, *CPK* creatine phosphokinase, *CV* cardiovascular, *EOW* every other week, *L* liter, *MTX* methotrexate, *OR* odds ratio, *QD* once daily, *RF* rheumatoid factor, *ULN* upper limit of normal, *UPA* upadacitinib

Supplementary Fig. S2. Patients with Grade 3 and Grade 4 levels by 12-week time intervals through 60 weeks

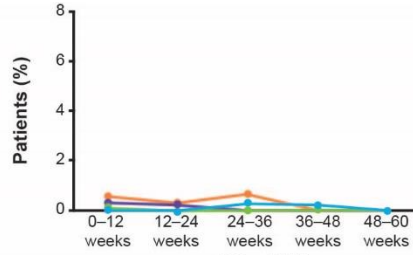


ALT



> 3.0 - 8.0 × ULN

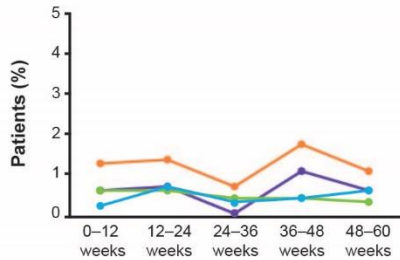
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	23/3193	30/3031	26/2738	16/2477	12/2294
UPA 30 mg QD	7/1193	16/1125	7/1003	8/956	10/862
ADA 40 mg EOW	2/326	3/420	0/461	5/368	3/321
MTX monotherapy	4/312	8/286	8/267	8/222	4/179



> 8.0 × ULN

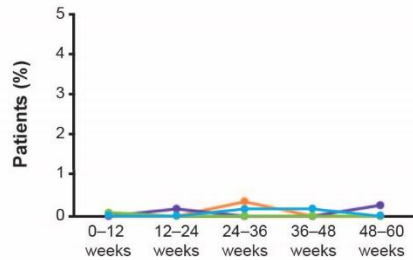
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	4/3193	3/3031	2/2738	1/2477	1/2294
UPA 30 mg QD	0/1193	1/1125	3/1003	2/956	0/862
ADA 40 mg EOW	1/326	1/420	0/461	0/368	0/321
MTX monotherapy	2/312	1/286	2/267	0/222	0/179

AST



> 3.0 - 8.0 × ULN

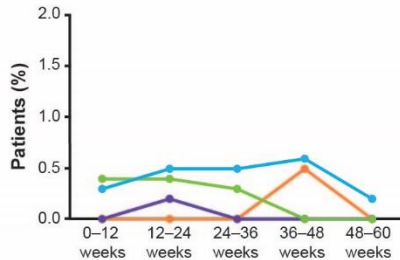
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	18/3193	19/3030	12/2735	10/2468	6/2283
UPA 30 mg QD	2/1192	8/1123	3/1002	4/956	5/859
ADA 40 mg EOW	2/326	3/420	0/461	4/367	2/321
MTX monotherapy	4/312	4/286	2/267	4/222	2/178



> 8.0 × ULN

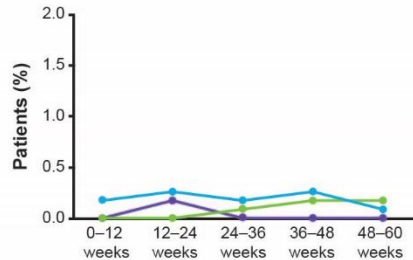
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	4/3193	2/3030	1/2735	0/2468	1/2283
UPA 30 mg QD	0/1192	0/1123	2/1002	2/956	0/859
ADA 40 mg EOW	0/326	1/420	0/461	0/367	1/321
MTX monotherapy	0/312	0/286	1/267	0/222	0/178

CPK^b



> 5.0 - 10.0 × ULN

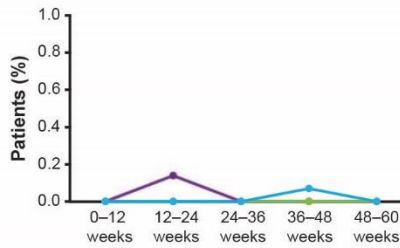
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	14/3193	13/3031	7/2734	2/2468	2/2278
UPA 30 mg QD	3/1194	6/1123	5/998	6/954	2/864
ADA 40 mg EOW	0/326	1/420	0/461	0/368	0/318
MTX monotherapy	0/312	0/286	0/266	1/222	0/177



> 10.0 × ULN

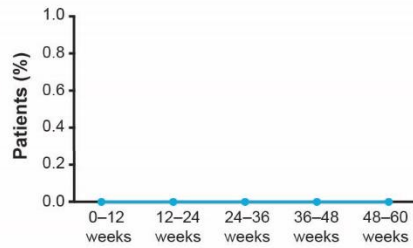
n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	3/3193	3/3031	3/2734	4/2468	4/2278
UPA 30 mg QD	2/1194	3/1123	2/998	3/954	1/864
ADA 40 mg EOW	0/326	1/420	0/461	0/368	0/318
MTX monotherapy	0/312	0/286	0/266	0/222	0/177

Creatinine^b



> 3.0 - 6.0 × ULN

n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	0/3194	1/3031	0/2744	0/2480	0/2297
UPA 30 mg QD	0/1196	0/1126	0/1003	1/958	0/862
ADA 40 mg EOW	0/326	1/420	0/462	0/368	0/321
MTX monotherapy	0/312	0/286	0/267	0/222	0/178



> 6.0 × ULN

n/N	0-12 weeks	12-24 weeks	24-36 weeks	36-48 weeks	48-60 weeks
UPA 15 mg QD	0/3194	1/3031	0/2744	0/2480	0/2297
UPA 30 mg QD	0/1196	0/1126	0/1003	0/958	0/862
ADA 40 mg EOW	0/326	0/420	0/462	0/368	0/321
MTX monotherapy	0/312	0/286	0/267	0/222	0/178

^aToxicity grading scale is based on OMERACT criteria. Post-baseline Grade must be higher than baseline Grade. ^bNational Cancer Institute standard common terminology criteria grading methodology was used. Post-baseline Grade must be higher than baseline Grade

ACPA anti-cyclic citrullinated protein antibody, *ADA* adalimumab, *BMI* body mass index, *CPK* creatine phosphokinase, *CV* cardiovascular, *EOW* every other week, *L* liter, *MTX* methotrexate, *OR* odds ratio, *QD* once daily, *RF* rheumatoid factor, *ULN* upper limit of normal, *UPA* upadacitinib

Supplementary Table. S1. Overview of the SELECT phase 3 clinical program for upadacitinib^a

Study	SELECT- EARLY	SELECT- NEXT	SELECT- MONOTHERAPY	SELECT- COMPARE	SELECT- BEYOND	SELECT- CHOICE
Patients	MTX-naïve	csDMARD-IR	MTX-IR	MTX-IR	bDMARD-IR	bDMARD-IR
Patients randomized	947	661	648	1629	499	613
Treatment groups	UPA 7.5 mg ^b UPA 15 mg UPA 30 mg MTX	UPA 15 mg UPA 30 mg PBO	UPA 15 mg UPA 30 mg MTX	UPA 15 mg ADA 40 mg PBO	UPA 15 mg UPA 30 mg PBO	UPA 15 mg ABA ^c
Background treatment	—	csDMARDs	—	MTX	csDMARDs	csDMARDs
Duration of study	5 years	5 years	5 years	10 years	5 years	5 years
ANALYSIS SET^{d,e}						
MTX monotherapy (N = 314)	✓	—	—	—	—	—
ADA 40 mg EOW + MTX (N = 579)	—	—	—	✓	—	—
UPA 15 mg QD (N = 3209)	✓	✓	✓	✓	✓	✓
UPA 30 mg QD (N = 1204)^f	✓	✓	✓	—	✓	—

^aTable adapted from Kakehasi A, et al. Clin Rheumatol 2023;42:1249–58. ^bJapanese patients only. ^cAll patients receiving ABA switched to UPA 15 mg QD at 24 weeks, therefore long-term data are not available for this treatment group. Intravenous ABA was administered at day 1 and weeks 2, 4, 8, 12, 16, and 20

(500 mg in patients with a body weight of < 60 kg, 750 mg in those with a weight of 60 to 100 kg, and 1000 mg in those with a weight of > 100 kg). ^dCut-off date was August 15, 2022. ^eTick mark indicates inclusion in the analysis set. ^fFollowing a protocol amendment due to the approval of the upadacitinib 15 mg dose, patients receiving upadacitinib 30 mg were switched to the 15 mg dose (earliest switch at week 108 [SELECT-EARLY]/168 [SELECT-NEXT]/132 [SELECT-MONOTHERAPY]/180 [SELECT-BEYOND])

ABA abatacept, *ADA* adalimumab, *bDMARD* biologic disease-modifying antirheumatic drug, *csDMARD* conventional synthetic disease-modifying antirheumatic drug, *EOW* every other week, *IR* inadequate responder, *MTX* methotrexate, *PBO* placebo, *PY* patient-years, *QD* once daily, *RA* rheumatoid arthritis, *UPA* upadacitinib