Supplementary Material

Routine Assessment of Patient Index Data 3 (RAPID3) in Patients with Rheumatoid Arthritis Treated with Long-Term Upadacitinib Therapy in Five Randomized Controlled Trials

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Supplementary Table S1 Overview of the patient populations/study designs of the SELECT trials

	SELECT-EARLY [10]	SELECT-NEXT [8]	SELECT-COMPARE [12]	SELECT-MONOTHERAPY [11]	SELECT-BEYOND [9]
Patients	MTX-naïve	csDMARD-IR	MTX-IR	MTX-IR	bDMARD-IR
Overall number of patients	945	661	1629	648	498
Background treatment	–	csDMARDs	MTX	–	csDMARDs
Active comparators	MTX	NA	ADA	Continued prior MTX	NA
Arms	UPA 15 mg UPA 30 mg MTX	UPA 15 mg UPA 30 mg PBO	UPA 15 mg ADA 40 mg PBO	UPA 15 mg UPA 30 mg PBO	UPA 15 mg UPA 30 mg PBO
Study duration	48 weeks	12 weeks	48 weeks	14 weeks	12 weeks
Total duration of study	5 years	5 years	10 years	5 years	5 years
Inclusion criteria	• Adults • Active RA • Symptoms consistent with RA ≥ 6 weeks • Fulfilled ACR/EULAR 2010 criteria for RA • MTX-naïve or ≤ 3 weekly MTX doses with ≥ 4-week washout before first dose of study drug	• Adults • Active RA for ≥ 3 months • Fulfilled ACR/EULAR 2010 criteria for RA • Had received up to 2 concomitant csDMARDs, with IR to MTX, SSZ, or LEF	• Adults • Active RA for ≥ 3 months • Fulfilled ACR/EULAR 2010 criteria for RA • Were on MTX ≥ 3 months	• Adults • Active RA despite MTX • Fulfilled ACR/EULAR 2010 criteria for RA • Had received MTX ≥ 3 months	• Adults • Active RA for ≥ 3 months despite treatment with ≥ 1 bDMARD for ≥ 3 months/or had intolerance to bDMARDs • Fulfilled ACR/EULAR 2010 criteria for RA

ACR American College of Rheumatology, *ADA* adalimumab, *bDMARD* biologic disease-modifying antirheumatic drug, *csDMARD* conventional synthetic disease-modifying antirheumatic drug, *EULAR* European Alliance of Associations for Rheumatology, *IR* inadequate response, *LEF* leflunomide, *MTX* methotrexate, *NA* not applicable, *PBO* placebo, *RA* rheumatoid arthritis, *SSZ* sulfasalazine, *UPA* upadacitinib

Supplementary Table S2 Mean baseline RAPID3 scores by study

	SELECT-EARLY			SELECT-NEXT		SELECT-COMPARE		SELECT-MONOTHERAPY		SELECT-BEYOND	
	MTX	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**ADA 40 mg EOW**	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**UPA 30 mg QD**
Patient (***N***)	313	317	314	221	219	651	327	216	215	163	161
Mean (SD) RAPID3 baseline scores	18.5 (5.6)	18.9 (5.6)	18.2 (5.6)	17.7 (5.1)	17.6 (5.3)	18.5 (5.5)	18.7 (5.4)	17.4 (5.8)	17.2 (5.9)	19.2 (5.1)	18.5 (5.3)

ADA adalimumab, *EOW* every other week, *MTX* methotrexate, *QD* once daily, *RAPID3* Routine Assessment of Patient Index Data 3, *SD* standard deviation, *UPA* upadacitinib

Supplementary Table S3 Kappa scores for RAPID3 remission correlations at week 60 with CDAI, SDAI, DAS28(CRP), and Boolean remission (all NRI)

	SELECT-EARLY			SELECT-NEXT		SELECT-COMPARE		SELECT-MONOTHERAPY		SELECT-BEYOND	
	MTX	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**ADA 40 mg EOW**	**UPA 15 mg QD**	**UPA 30 mg QD**	**UPA 15 mg QD**	**UPA 30 mg QD**
CDAI	0.65***	0.67***	0.64***	0.58***	0.52***	0.66***	0.76***	0.53***	0.54***	0.59***	0.59***
SDAI	0.65***	0.64***	0.61***	0.63***	0.54***	0.68***	0.77***	0.58***	0.51***	0.59***	0.53***
DAS28(CRP)	0.53***	0.54***	0.54***	0.52***	0.49***	0.60***	0.65***	0.46***	0.40***	0.35***	0.53***
Boolean	0.68***	0.72***	0.67***	0.64***	0.59***	0.68***	0.70***	0.53***	0.54***	0.58***	0.54***

***$p < 0.001$.

ADA adalimumab, *CDAI* Clinical Disease Activity Index, *DAS28(CRP)* 28-joint Disease Activity Score using C-reactive protein, *EOW* every other week, *MTX* methotrexate, *NRI* non-responder imputation, *QD* once daily, *RAPID3* Routine Assessment of Patient Index Data 3, *SDAI* Simplified Disease Activity Index, *UPA* upadacitinib

Supplementary Table S4 (A) Odds ratios (95% CI) and (B) C-indices (95% CI) from univariate logistic regression of associations between RAPID3 disease activity and change from baseline at week 12 or 14 with CDAI remission and Boolean remission at week 60 for patients who received upadacitinib 15 mg once daily

(A)

RAPID3 assessment at week 12/14	CDAI remission at week 60					Boolean remission at week 60				
	SELECT-EARLY	SELECT-NEXT	SELECT-COMPARE	SELECT-MONOTHERAPY	SELECT-BEYOND	SELECT-EARLY	SELECT-NEXT	SELECT-COMPARE	SELECT-MONOTHERAPY	SELECT BEYOND
RAPID3 score	0.85 (0.81–0.90)	0.86 (0.81–0.92)	0.83 (0.80–0.87)	0.82 (0.76–0.88)	0.85 (0.79–0.93)	0.84 (0.79–0.89)	0.86 (0.80–0.93)	0.81 (0.77–0.84)	0.82 (0.75–0.90)	0.85 (0.77–0.93)
RAPID3 change from baseline	0.94 (0.91–0.97)	0.87 (0.82–0.92)	0.93 (0.90–0.95)	0.87 (0.83–0.92)	0.93 (0.87–1.00)	0.94 (0.90–0.97)	0.88 (0.83–0.93)	0.91 (0.88–0.94)	0.94 (0.89–0.99)	0.95 (0.88–1.02)
Remission	5.33 (2.97–9.57)	3.15 (1.55–6.41)	6.96 (4.37–11.07)	7.65 (3.33–17.58)	8.98 (3.11–25.94)	7.05 (3.91–12.72)	3.75 (1.81–7.77)	8.80 (5.51–14.06)	7.74 (3.30–18.16)	5.39 (1.86–15.61)
LDA	1.29 (0.69–2.39)	1.94 (0.82–4.59)	1.95 (1.23–3.08)	2.21 (0.97–5.02)	0.72 (0.15–3.47)	0.99 (0.52–1.92)	1.63 (0.67–3.97)	1.81 (1.12–2.91)	1.91 (0.76–4.80)	1.91 (0.48–7.64)
MDA	0.77 (0.45–1.34)	0.82 (0.41–1.63)	0.72 (0.48–1.08)	0.48 (0.23–1.02)	0.93 (0.36–2.45)	0.62 (0.34–1.13)	0.70 (0.33–1.48)	0.63 (0.40–0.98)	0.20 (0.06–0.69)	1.15 (0.41–3.26)
HDA	0.15 (0.07–0.31)	0.19 (0.08–0.48)	0.15 (0.08–2.24)	0.18 (0.08–0.43)	0.26 (0.10–0.69)	0.12 (0.05–0.30)	0.18 (0.06–0.52)	0.09 (0.05–0.18)	0.23 (0.08–0.69)	0.15 (0.04–0.55)

(B)

RAPID3 assessment at week 12/14	CDAI remission at week 60					Boolean remission at week 60				
	SELECT-EARLY	SELECT-NEXT	SELECT-COMPARE	SELECT-MONOTHERAPY	SELECT-BEYOND	SELECT-EARLY	SELECT-NEXT	SELECT-COMPARE	SELECT-MONOTHERAPY	SELECT-BEYOND
RAPID3 score	0.75 (0.69–0.80)	0.72 (0.64–0.80)	0.77 (0.73–0.82)	0.79 (0.72–0.86)	0.76 (0.66–0.87)	0.76 (0.70–0.82)	0.73 (0.64–0.81)	0.81 (0.77–0.85)	0.79 (0.70–0.88)	0.77 (0.67–0.88)
RAPID3 change from baseline	0.63 (0.56–0.69)	0.74 (0.66–0.82)	0.65 (0.60–0.70)	0.74 (0.66–0.81)	0.62 (0.50–0.75)	0.63 (0.55–0.70)	0.73 (0.63–0.82)	0.68 (0.63–0.73)	0.64 (0.54–0.74)	0.59 (0.46–0.72)
Remission	0.66 (0.61–0.72)	0.61 (0.54–0.69)	0.66 (0.62–0.70)	0.67 (0.60–0.74)	0.67 (0.57–0.77)	0.70 (0.64–0.76)	0.64 (0.56–0.72)	0.69 (0.65–0.74)	0.70 (0.61–0.79)	0.65 (0.53–0.76)
LDA	0.52 (0.47–0.57)	0.54 (0.48–0.60)	0.55 (0.51–0.58)	0.56 (0.49–0.62)	0.51 (0.45–0.57)	0.50 (0.45–0.55)	0.53 (0.47–0.60)	0.54 (0.51–0.58)	0.55 (0.47–0.63)	0.53 (0.45–0.62)
MDA	0.53 (0.47–0.58)	0.52 (0.45–0.59)	0.53 (0.49–0.57)	0.57 (0.50–0.64)	0.51 (0.41–0.60)	0.55 (0.49–0.60)	0.54 (0.46–0.61)	0.55 (0.50–0.59)	0.62 (0.56–0.69)	0.51 (0.40–0.63)
HDA	0.66 (0.61–0.70)	0.64 (0.58–0.70)	0.68 (0.64–0.71)	0.66 (0.59–0.72)	0.65 (0.56–0.75)	0.65 (0.61–0.70)	0.63 (0.57–0.69)	0.69 (0.66–0.72)	0.63 (0.56–0.70)	0.69 (0.60–0.78)

CDAI Clinical Disease Activity Index, *CI* confidence interval, *HDA* high disease activity, *LDA* low disease activity, *MDA* moderate disease activity, *RAPID3* Routine Assessment of Patient Index Data 3

Supplementary Table S5 Spearman correlations (95% CIs) between RAPID3 component scores and disease activity measures (as observed) at week 60

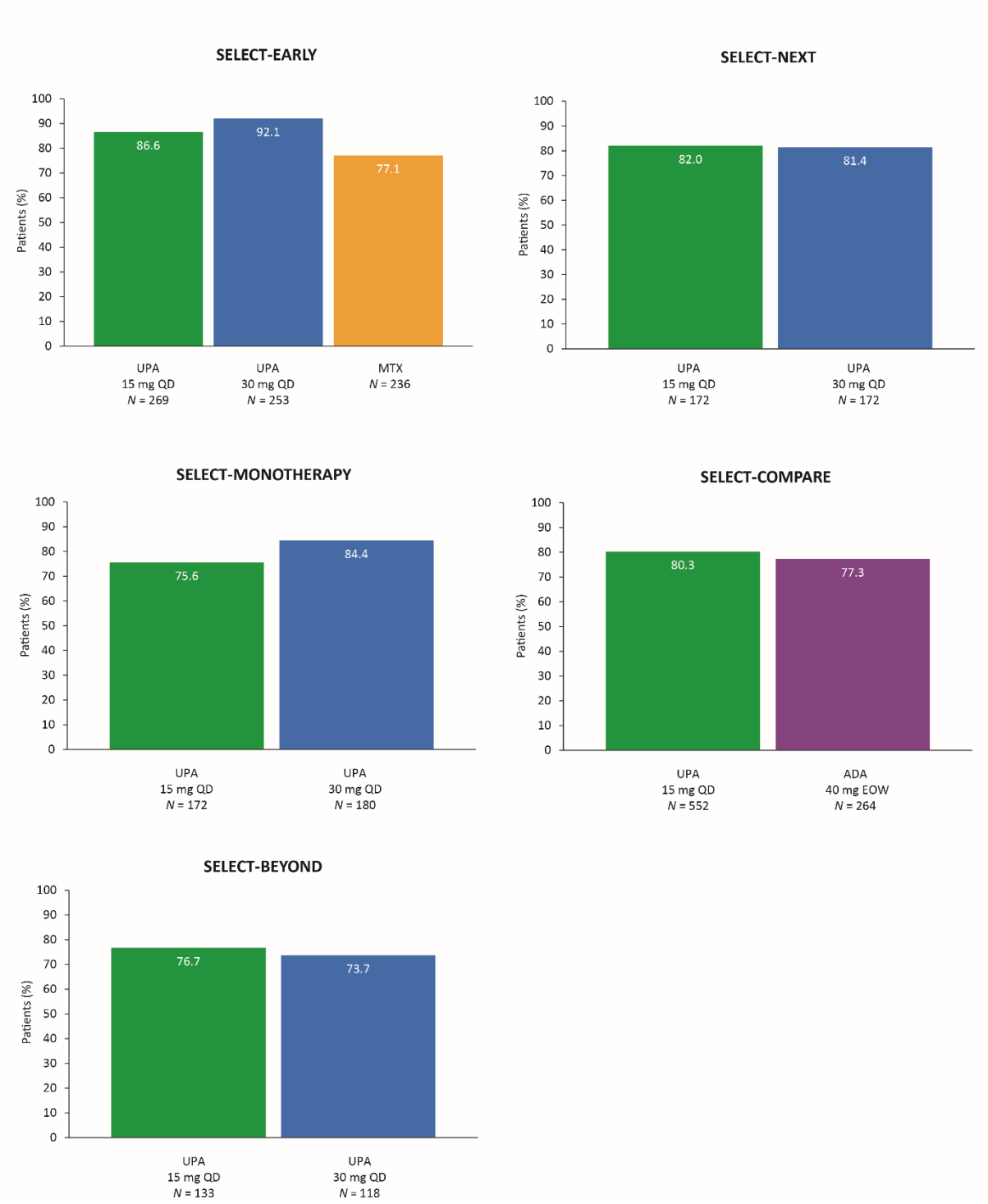
	MTX	UPA 15 mg QD	UPA 30 mg QD	UPA 15 mg QD	UPA 30 mg QD	ADA 40 mg EOW	UPA 15 mg QD	UPA 15 mg QD	UPA 30 mg QD	UPA 15 mg QD	UPA 30 mg QD
PtGA											
CDAI	0.78 (0.72–0.82)***	0.82 (0.77–0.85)***	0.79 (0.74–0.84)***	0.73 (0.66–0.80)***	0.76 (0.69–0.82)***	0.74 (0.68–0.79)***	0.81 (0.78–0.84)***	0.79 (0.72–0.84)***	0.74 (0.67–0.80)***	0.71 (0.61–0.78)***	0.77 (0.69–0.84)***
DAS28(CRP)	0.71 (0.64–0.77)***	0.70 (0.64–0.76)***	0.64 (0.57–0.71)***	0.69 (0.61–0.76)***	0.66 (0.56–0.73)***	0.72 (0.66–0.78)***	0.76 (0.72–0.80)***	0.69 (0.60–0.76)***	0.60 (0.50–0.69)***	0.64 (0.52–0.73)***	0.71 (0.60–0.79)***
SDAI	0.78 (0.72–0.83)***	0.81 (0.76–0.85)***	0.76 (0.70–0.81)***	0.74 (0.66–0.80)***	0.74 (0.66–0.80)***	0.73 (0.67–0.79)***	0.80 (0.77–0.83)***	0.79 (0.72–0.84)***	0.72 (0.65–0.79)***	0.71 (0.61–0.79)***	0.75 (0.66–0.82)***
TJC28	0.52 (0.42–0.60)***	0.51 (0.42–0.59)***	0.50 (0.40–0.59)***	0.48 (0.36–0.59)***	0.51 (0.39–0.61)***	0.54 (0.45–0.62)***	0.62 (0.57–0.67)***	0.41 (0.28–0.53)***	0.37 (0.24–0.49)***	0.34 (0.18–0.48)***	0.56 (0.43–0.67)***
SJC28	0.44 (0.33–0.54)***	0.39 (0.29–0.49)***	0.36 (0.25–0.46)***	0.33 (0.19–0.45)***	0.32 (0.18–0.45)***	0.45 (0.35–0.54)***	0.46 (0.39–0.52)***	0.25 (0.10–0.38)***	0.16 (0.01–0.30)*	0.11 (–0.06–0.27)	0.26 (0.09–0.42)**
HAQ-DI functional component											
CDAI	0.59 (0.50–0.67)***	0.66 (0.59–0.73)***	0.57 (0.48–0.65)***	0.44 (0.31–0.55)***	0.52 (0.40–0.62)***	0.60 (0.52–0.67)***	0.66 (0.61–0.70)***	0.61 (0.50–0.69)***	0.45 (0.32–0.56)***	0.51 (0.37–0.62)***	0.48 (0.33–0.61)***
DAS28(CRP)	0.59 (0.50–0.67)***	0.63 (0.55–0.70)***	0.53 (0.43–0.61)***	0.46 (0.34–0.57)***	0.50 (0.38–0.61)***	0.61 (0.53–0.69)***	0.64 (0.59–0.69)***	0.59 (0.48–0.68)***	0.38 (0.25–0.50)***	0.50 (0.36–0.61)***	0.43 (0.27–0.57)***
SDAI	0.60 (0.51–0.68)***	0.66 (0.59–0.72)***	0.55 (0.46–0.63)***	0.46 (0.33–0.57)***	0.54 (0.42–0.64)***	0.61 (0.53–0.68)***	0.66 (0.61–0.70)***	0.61 (0.50–0.69)***	0.43 (0.30–0.54)***	0.51 (0.37–0.63)***	0.44 (0.28–0.58)***
TJC28	0.49 (0.38–0.58)***	0.55 (0.46–0.63)***	0.44 (0.33–0.53)***	0.37 (0.24–0.49)***	0.45 (0.32–0.56)***	0.52 (0.43–0.60)***	0.59 (0.53–0.64)***	0.53 (0.41–0.63)***	0.32 (0.19–0.45)***	0.39 (0.23–0.52)***	0.49 (0.35–0.62)***
SJC28	0.37 (0.25–0.47)***	0.44 (0.34–0.53)***	0.34 (0.22–0.44)***	0.22 (0.07–0.35)**	0.23 (0.09–0.37)**	0.44 (0.33–0.53)***	0.41 (0.34–0.48)***	0.29 (0.14–0.42)***	0.06 (–0.09–0.20)	0.07 (–0.10–0.24)	0.12 (–0.06–0.29)
Pain											

CDAI	0.75 (0.68–0.80)***	0.78 (0.72–0.82)***	0.76 (0.70–0.81)***	0.73 (0.65–0.79)***	0.71 (0.63–0.78)***	0.73 (0.67–0.79)***	0.80 (0.77–0.83)***	0.72 (0.64–0.79)***	0.70 (0.62–0.77)***	0.66 (0.55–0.75)***	0.75 (0.66–0.82)***
DAS28(CRP)	0.69 (0.61–0.75)***	0.69 (0.62–0.75)***	0.61 (0.53–0.68)***	0.68 (0.60–0.76)***	0.63 (0.53–0.72)***	0.73 (0.67–0.78)***	0.76 (0.72–0.79)***	0.67 (0.57–0.74)***	0.58 (0.47–0.67)***	0.62 (0.50–0.72)***	0.71 (0.60–0.79)***
SDAI	0.75 (0.69–0.80)***	0.77 (0.72–0.82)***	0.73 (0.66–0.78)***	0.73 (0.66–0.80)***	0.70 (0.61–0.77)***	0.73 (0.67–0.79)***	0.79 (0.76–0.82)***	0.73 (0.65–0.79)***	0.68 (0.60–0.76)***	0.66 (0.55–0.75)***	0.73 (0.63–0.81)***
TJC28	0.52 (0.42–0.61)***	0.57 (0.48–0.64)***	0.49 (0.39–0.57)***	0.49 (0.37–0.60)***	0.50 (0.38–0.60)***	0.58 (0.50–0.66)***	0.64 (0.59–0.69)***	0.49 (0.37–0.60)***	0.41 (0.28–0.52)***	0.37 (0.21–0.51)***	0.62 (0.50–0.72)***
SJC28	0.42 (0.31–0.52)***	0.45 (0.35–0.54)***	0.38 (0.27–0.48)***	0.36 (0.22–0.48)***	0.29 (0.15–0.42)***	0.47 (0.38–0.56)***	0.45 (0.39–0.52)***	0.22 (0.07–0.35)**	0.20 (0.06–0.34)**	0.18 (0.01–0.34)*	0.30 (0.13–0.45)***

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

ADA adalimumab, *CDAI* Clinical Disease Activity Index, *CI* confidence interval, *DAS28(CRP)* 28-joint Disease Activity Score using C-reactive protein, *EOW* every other week, *HAQ-DI* Health Assessment Questionnaire Disability Index, *MTX* methotrexate, *PtGA* Patient Global Assessment of Disease Activity, *QD* once daily, *RAPID3* Routine Assessment of Patient Index Data 3, *SDAI* Simplified Disease Activity Index, *SJC28* swollen joint count for 28 joints, *TJC28* tender joint count for 28 joints, *UPA* upadacitinib

Supplementary Fig. S1 Percentage of patients reporting improvements in RAPID3 beyond the MCID at week 60



Data are as observed.
ADA adalimumab, *EOW* every other week, *MCID* minimal clinically important difference, *MTX* methotrexate, *QD* once daily, *RAPID3* Routine Assessment of Patient Index Data 3, *UPA* upadacitinib