Online Resource Table 2

Upadacitinib in Rheumatoid Arthritis: A Benefit–Risk Assessment Across a Phase III Program

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Online Resource Table 2 Summary of patient-reported outcomes across upadacitinib clinical trials[a]

Study	SELECT-EARLY[b]		SELECT-NEXT[c]		SELECT-COMPARE[d]			SELECT-MONOTHERAPY[c]		SELECT-BEYOND[c]	
Patient populations	MTX-naïve		csDMARD-IR		MTX-IR			MTX-IR		bDMARD-IR	
References	[1, 2]		[3, 4]		[5, 6]			[7, 8]		[9, 10]	
Arms	MTX	UPA 15 mg	PBO → UPA 15 mg	UPA 15 mg	PBO + MTX	UPA 15 mg + MTX	ADA 40 mg + MTX	MTX → UPA 15 mg	UPA 15 mg	PBO → UPA 15 mg	UPA 15 mg
N	314	317	221	221	651	651	327	216	217	169	164
Least mean square change from baseline in HAQ-DI											
week 12[e]/14[f]	−0.5 (*n* = 313)	−0.8[***]	−0.3	−0.6[††††]	−0.3	−0.6[††††‖‡‡]	−0.5	−0.3	−0.7[***]	−0.2	−0.4[††††]
week 24[g]/26[h]	−0.6 (*n* = 313)	−0.9[***]	—	—	—	—	—	—	—	—	—
week 48[i]/60[j]	−0.74	−0.96***	−0.79	−0.83	—	−0.7‡‡	−0.6	−0.69	−0.73	−0.52	−0.52
Decrease from baseline in HAQ-DI ≥ 0.22 (MCID)											

week 12[e]/14[f]	—	—	49.3	73.6[††††] (*n* = 212)	—	—	—	47.8 (*n* = 205)	65.7[****] (*n* = 213)	—	—
week 24[g]/26[h]	61.0 (*n* = 307)	77.0[***] (*n* = 308)	—	—	—	—	—	—	—	—	—
week 48[i]/60[k]	—	—	—	—	—	62[‡‡]	52	—	—	66.7 (*n* = 60)	70.0 (*n* = 130)
Least mean square change from baseline in SF-36 PCS											
week 12[e]/14[f]	5.7 (*n* = 311)	10.0[[**]] (*n* = 315)	3.0 (*n* = 207)	7.6[[††††]] (*n* = 209)	3.6	7.9[[†††]‡‡]	6.3	4.3	8.3[[***]]	2.4	5.8[[††††]]
week 24[g]/26[h]	7.0 (*n* = 313)	10.7[[**]] (*n* = 315)	—	—	4.5	9.5[††††‡‡]	7.8	—	—	—	—
week 48	—	—	—	—	—	9.8[‡‡]	8.1	—	—	—	—
Least mean square change from BL in morning stiffness duration, min											
week 12[e]/14[f]	−72.4 (*n* = 278)	−106.0[***] (*n* = 301)	−34.3	−85.3[[†††]]	−50.4	−93.0[[†††]]	−84.0	−53.0	−94.6[[**]]	−15.1	−81.5[†††]
week 24[g]/26[h]	−87.9 (*n* = 266)	−114.6[***] (*n* = 287)	—	—	−53.9	−100.3[†††]	−91.4	—	—	—	—

week 48	—	—	—	—	—	−101.7	−95.5	—	—	—	—
Least mean square change from baseline in FACIT-F											
week 12[e]/14[f]	6.8 (*n* = 277)	10.0[***] (*n* = 301)	3.0 (*n* = 207)	7.9[[††††]] (*n* = 207)	4.8	9.0[[†††]‡]	7.4	—	—	—	—
week 24[g]/26[h]	7.4 (*n* = 268)	10.6[***] (*n* = 289)	—	—	5.5	9.7[†††‡]	8.2	—	—	—	—
week 48	8.5	10.1[#]	—	—	—	10.2[‡]	8.9	—	—	—	—
Least mean square change in patient's assessment of pain											
week 12[e]/14[f]	−25.4 (*n* = 278)	−36.3[***] (*n* = 302)	−10.3	−29.9[††††]	−15.7	−32.1[[†††]‡‡‡]	−25.6	−13.9	−26.2[****]	—	—
week 24[g]/26[h]	−28.4 (*n* = 266)	−39.8[***] (*n* = 288)	—	—	—	—	—	—	—	—	—
week 48	—	—	—	—	—	−36.7[‡]	−32.1	—	—	—	—

ADA adalimumab, *bDMARD* biologic disease-modifying antirheumatic drug, *BL* baseline, *csDMARD* conventional synthetic disease-modifying antirheumatic drug, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *IR* inadequate responder, *LOCF* last observation carried forward, *MCID* minimal clinically important difference, *MTX* methotrexate, *NRI* non-responder imputation, *PBO* placebo, *PCS* physical component summary, *SF-36* Short Form-36 Physical Component Summary, *UPA* upadacitinib

[a]Missing data were imputed using: NRI for binary outcomes or mixed-model repeated measures with observed data for continuous outcomes, unless otherwise stated

[b]Multiple imputation and LOCF for continuous outcomes

[c]Week 48/60 data are reported as observed

[d]Binary outcomes analyzed by NRI for observations after rescue for patients rescued at weeks 14, 18, or 22; LOCF for observations after rescue for patients rescued at week 26; and continuous outcomes analyzed by LOCF for observations after rescue for patients rescued at weeks 14–26

[e]SELECT-EARLY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND

[f]SELECT-MONOTHERAPY

[g]SELECT-EARLY

[h]SELECT-COMPARE

[i]SELECT-EARLY, SELECT-COMPARE, and SELECT-MONOTHERAPY

[j]SELECT-NEXT and SELECT-BEYOND

[k]SELECT-BEYOND

Comparisons adjusted for multiplicity: $^{[**]}p \leq 0.01$, $^{[***]}p \leq 0.001$ vs MTX; $^{[\dagger\dagger\dagger]}p \leq 0.001$, $^{[\dagger\dagger\dagger\dagger]}p \leq 0.0001$ vs placebo; $^{[\ddagger\ddagger]}p \leq 0.01$, $^{[\ddagger\ddagger\ddagger]}p \leq 0.001$ vs ADA

Comparisons unadjusted for multiplicity: Nominal $^{\#}p = 0.058$, $^{***}p \leq 0.001$, $^{****}p \leq 0.0001$ vs MTX; $^{\dagger\dagger\dagger}p \leq 0.001$, $^{\dagger\dagger\dagger\dagger}p \leq 0.0001$ vs PBO; $^{\ddagger}p \leq 0.05$, $^{\ddagger\ddagger}p \leq 0.01$ vs ADA

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