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SAT0255

PATIENT REPORTED OUTCOMES OF UPADACITINIB: RESULTS FROM BIOLOGIC INADEQUATE RESPONDERS (SELECT BEYOND PHASE III TRIAL)

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Background: Patient reported outcomes (PROs) were studied in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease modifying anti-rheumatic drugs (bDMARD-IR) in a trial of upadacitinib (UPA), a selective JAK-1 inhibitor. Improvements in PROs are important when evaluating comprehensive efficacy of treatments for RA.

Objectives: The objective of this post-hoc analysis was to compare PRO responses and numbers needed to treat (NNT) in order to assess clinically meaningful improvements in bDMARD-IR patients with RA receiving UPA.

Methods: Data from the SELECT BEYOND randomised controlled trial (RCT) (NCT02706847) were used to compare PRO responses between UPA (15 mg QD and 30 mg QD) and PBO. PROs included physical function by Health Assessment Questionnaire Disability Index (HAQ-DI), Patient's Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), pain by VAS, duration and severity of morning (AM) stiffness, health-related quality of life by Short Form 36 Health Survey (SF-36), and severity of insomnia by Insomnia Severity Index (ISI). Changes in least squares means (LSM) from baseline to week 12 were based on mixed effect repeated measures models. Percentages of patients reporting changes in PRO scores from baseline to week 12 ≥ minimum clinically important difference (MCID) values or scores ≥ normative values (age- and gender-matched for SF-36 only) were determined; comparisons between groups used chi-square tests. For each PRO measure, the incremental NNT to achieve clinically meaningful improvements from baseline (≥ MCID) was calculated.

Abstract SAT0255 – Table 1. LSM Changes From Baseline and Percentage of Responders at Week 12

PRO	Change from Baseline			% Responders					
	LSM			Reporting Scores ≥ MCID, n (%)			Reporting Scores ≥ Normative Values, n (%)		
	PBO N=169	UPA 15mg N=164	UPA 30mg N=165	PBO N=169	UPA 15mg N=164	UPA 30mg N=165	PBO N=169	UPA 15mg N=164	UPA 30mg N=165
HAQ-DI	-0.16	-0.41*	-0.44*	61 (36.6)	102 (62.6)*	89 (53.3)*	11 (6.6)	26 (16.0)*	21 (13.0)
PtGA	-10.03	-26.04*	-29.27*	71 (42.8)	119 (73.0)*	101 (62.0)*	25 (15.5)	46 (28.2)*	58 (35.6)*
Pain VAS	-10.38	-25.91*	-30.92*	76 (45.8)	120 (73.6)*	103 (64.0)*	—	—	—
Duration AM Stiffness ^a	-15.07	81.47*	-79.13*	17 (10.1)	33 (20.1)* ^b	40 (24.2)*	—	—	—
Severity AM Stiffness ^a	-1.57	-2.86*	-3.22*	95 (56.2)	131 (79.9)* ^b	119 (72.1)*	—	—	—
SF-36 PCS	2.39	5.83*	7.02*	65 (39.2)	98 (60.1)*	104 (64.2)*	9 (5.4)	18 (11.0)	24 (14.8)*
SF-36 MCS	3.01	4.54	3.37	72 (43.4)	88 (54.0)	77 (47.5)	73 (44.0)	88 (54.0)	78 (48.1)
SF-36 PF	1.54	4.56*	6.15*	78 (46.2)	103 (62.8)*	107 (64.8)*	16 (9.5)	25 (15.9)	23 (13.9)
SF-36 RP	2.15	5.10*	5.17*	73 (43.2)	101 (61.6)*	101 (61.2)*	12 (7.1)	24 (14.6)*	24 (14.5)*
SF-36 BP	4.71	8.12*	9.09*	91 (53.8)	120 (73.2)*	111 (67.3)*	19 (11.2)	39 (23.8)*	40 (24.2)*
SF-36 GH	2.17	4.31*	4.25*	71 (42.0)	104 (63.4)*	97 (58.8)*	24 (14.2)	29 (17.7)	27 (16.4)
SF-36 VT	3.10	6.28*	6.86*	86 (50.9)	108 (65.9)*	109 (66.1)*	33 (19.5)	50 (30.5)	46 (27.9)
SF-36 SF	3.45	5.87*	5.35*	81 (47.9)	103 (62.8)*	79 (47.9)	42 (24.9)	50 (30.5)	49 (29.7)
SF-36 RE	2.66	4.72*	3.78	61 (36.1)	84 (51.2)*	66 (40.0)	55 (32.5)	67 (40.9)	61 (37.0)
SF-36 MH	2.96	3.83	3.53	80 (47.3)	92 (56.1)	86 (52.1)	56 (33.1)	72 (43.9)	61 (37.0)
ISI	-1.69	-2.53	-3.32*	12 (7.8)	22 (14.5)	24 (15.9)*	50 (32.7)	57 (37.5)	67 (44.4)*

*P<0.05 for UPA vs PBO.

^aDuration in minutes; ^b% responders reporting scores ≥ minimal important differences. ^cAssessed on a numeric scale of 1–10 with 10 being the worst level.

BP: bodily pain; GH: general health; MCS: Mental Component Summary; MH: mental health; PCS: Physical Component Summary; PF: physical functioning; RE: role emotional; RP: role-physical; SF: social functioning; VT: vitality.

Results: Data from 498 patients (169 in PBO, 164 in UPA 15 mg, 165 in 30 mg UPA) were analysed. Mean age was 57 years, 84% were females, and 55% had RA for ≥10 years. Both UPA doses resulted in statistically significant LSM

changes from baseline vs PBO in HAQ-DI, PtGA, pain, duration and severity of AM stiffness, SF-36 Physical Component Summary (PCS), 7/8 domains (15 mg), and 6/8 domains (30 mg) (Table). Compared with PBO at week 12, UPA-treated patients reported higher responses that were statistically significant and clinically meaningful for HAQ-DI, PtGA, pain, duration and severity of AM stiffness, SF-36 PCS, 7/8 domains (15 mg), 5/8 domains (30 mg), and ISI (30 mg). The Table presents the proportion of patients reporting scores that were ≥ normative values at week 12. Across most PROs, the NNTs with UPA ranged from 4 to 7 patients.

Conclusions: This RCT demonstrated that even in difficult-to-treat bDMARD-IR patients with active RA, treatment with UPA resulted in significantly more patients with clinically meaningful improvements in PROs or responses that approached normative values. The NNT to achieve a meaningful response was favourable.

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SAT0256

TOFACITINIB WITH AND WITHOUT METHOTREXATE VERSUS ADALIMUMAB WITH METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: PATIENT-REPORTED OUTCOMES FROM A PHASE 3B/4 RANDOMISED TRIAL

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To compare patient-reported outcomes (PROs) among patients receiving tofacitinib monotherapy, tofacitinib +methotrexate (MTX) and adalimumab (ADA) +MTX, in a head-to-head trial of patients with RA and inadequate responses to MTX (MTX-IR).

Methods: ORAL Strategy (NCT02187055) was a Phase 3b/4, 1 year, triple dummy, active randomised controlled trial (RCT). Patients were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID+MTX (tofa +MTX) or subcutaneous ADA 40 mg every other week +MTX (ADA +MTX); MTX doses were 15–25 mg/wk. PROs (secondary endpoints in this RCT) assessed at Months (Mos) 6 and 12 included mean changes from baseline in: patient global assessment of disease activity (visual analogue scale [VAS]); arthritis pain (VAS); Health Assessment Questionnaire-Disability Index (HAQ-DI); Short Form-36 Health Survey; EuroQol 5-dimensions Questionnaire; Work Productivity and Activity Impairment Questionnaire; Functional Assessment of Chronic Illness Therapy-Fatigue; and the proportion of patients reporting improvements in HAQ-DI ≥ minimum clinically important difference (MCID; -0.22). Nominal p values were calculated with no adjustment for multiple comparisons.

Results: Among 1146 patients treated (tofa mono: n=384; tofa +MTX: n=376; ADA+MTX: n=386), baseline demographics and disease characteristics were comparable. At Mos 6 and 12, improvements in all PROs were similar for tofa +MTX and ADA+MTX (there were essentially no differences based on nominal p values) and numerically greater than with tofa mono (Table). Mean changes from baseline in HAQ-DI scores were similar in each treatment group at Mos 6 and 12; similar proportions reported improvements ≥ MCID.

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A PHASE 2B/3 RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF UPADACITINIB, A SELECTIVE JAK1 INHIBITOR, IN JAPANESE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS

Results: Of 197 patients treated, 187 completed the double-blind period. At Week 12, more patients receiving UPA 7.5, 15 and 30 mg vs PBO met ACR20 (75.5%, 83.7%, 80% vs 42.9%, $p<0.001$). A significant difference in ACR20 was observed as early as Week 1 (**table 1**). The more stringent responses, such as ACR50/70, DAS28-CRP ≤ 3.2 , were achieved by significantly higher proportions of patients on UPA vs PBO with more patients on UPA 15 mg and 30 mg achieving

Overall adverse events (AE), serious AEs, infections (including serious infections, opportunistic infections and herpes zoster) were numerically higher in UPA 30 mg. There were no events of pulmonary embolism, deep vein thrombosis, tuberculosis or malignancy and there were no deaths. Mean haemoglobin levels improved with UPA 7.5 (+0.35 g/dL) and remained stable with UPA 15 (-0.03 g/dL) vs UPA 30 (-0.54 g/dL) and PBO (-0.17 g/dL). CPK elevations and lymphopenia occurred more frequently in UPA 30 mg.

Conclusions: In this Japanese RA csDMARD-IR population, the efficacy of UPA was demonstrated, with better responses for more stringent endpoints on UPA 15 mg and 30 mg vs 7.5 mg. The frequency of overall AEs was numerically higher in UPA 30 mg. Overall, safety and tolerability were consistent with Phase 2 and 3 studies to date.

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