important to exert certain efficacy of MTX. We previously reported in retrospective study that MTX-PG concentration in RA patients keeping remission for long time was associated with several SNPs²), and some of the results were confirmed in this prospective study.

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SAT0239

RAPID RESPONSE WITH UPADACITINIB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CSDMARDS OR bDMARDS

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Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients (pts) with moderate to severe rheumatoid arthritis (RA) with an inadequate response (IR) to csDMARDs or bDMARDs in the SELECT-NEXT¹ and SELECT-BEYOND² trials, respectively.

Objectives: To investigate the speed of response to UPA across disease measures in csDMARD- and bDMARD-IR pts.

Methods: 661 pts in NEXT and 498 in BEYOND received UPA 15 mg or UPA 30 mg once daily (QD) or placebo (PBO) for 12 weeks (wks)^{1,2}. Time to first achievement of clinically meaningful outcomes, including ACR20/50, DAS28-CRP≤3.2 and Low Disease Activity (LDA) measures of CDAI (≤10) and SDAI (≤11) was evaluated. The cumulative incidences of ACR20/50, DAS28-CRP≤3.2 and LDA by CDAI and SDAI over 12 wks were estimated. Hazard ratios between UPA and PBO were obtained using Cox proportional hazards model with treatment group, corresponding baseline values and main stratification factors, without control for multiple comparisons. All analyses were based on observed data without imputation.

Table 1. Summary of Median Time (in Weeks) to Achieve First Response Over 12 Weeks

		csDMARD-IR			bDMARD-IR		
		N	Median (Q1, Q3)	HR	N	Median (Q1, Q3)	HR
ACR20	PBO	221	12.1 (2.9, NE)		169	11.9 (2.3, NE)	
	UPA 15	219	4.1 (2, 12.1)	2.1***	164	4.1 (1.3, 12.1)	2.0***
	UPA 30	216	2.4 (1.3, 8.1)	2.5***	164	2.7 (1.6, 12.1)	2.0***
ACR50	PBO	221	12.9 (2.4, NE)		169	NE (NE, NE)	
	UPA 15	219	12.3 (4.3, NE)	2.4***	164	12.7 (8, NE)	2.8***
	UPA 30	216	8.6 (4.1, 13.4)	3.4***	165	12.1 (4.1, NE)	3.6***
DAS28-CRP ≤3.2	PBO	221	NE (12.1, NE)		166	NE (12.2, NE)	
	UPA 15	214	12.1 (4.1, 13)	2.9***	163	12.2 (4.1, NE)	2.8***
	UPA 30	215	8.1 (2.6, 12.7)	3.9***	163	8.7 (4.1, 13)	3.2***
CDAI LDA	PBO	210	NE (12.1, NE)		159	NE (NE, NE)	
	UPA 15	206	12.3 (8, 13)	2.2***	156	13.1 (8.1, NE)	2.1***
	UPA 30	209	12.1 (4.1, 13.3)	2.6***	156	12.3 (4.3, NE)	2.5***
SDAI LDA	PBO	210	NE (12.1, NE)		160	NE (12.3, NE)	
	UPA 15	206	12.3 (4.1, 13)	2.6***	156	12.4 (7.7, NE)	2.2***
	UPA 30	209	12 (4.1, 13.4)	3.2***	156	12.1 (4.1, NE)	2.7***
TK68 50% Improvement	PBO	221	8.1 (2.3, NE)		169	8.1 (2.1, 12.4)	
	UPA 15	220	4.1 (2, 12.1)	1.6***	164	4.1 (1.3, 12.1)	1.5**
	UPA 30	216	4.1 (2.1, 8.6)	1.7***	165	4.1 (2, 8.4)	1.5**
SK66 50% Improvement	PBO	221	4.4 (2.1, 12.9)		169	4.1 (2.1, 12.3)	
	UPA 15	220	4.0 (1.4, 8.1)	1.5***	164	2.3 (1.3, 8.4)	1.4**
	UPA 30	216	2.2 (1.3, 8.1)	1.6***	165	3.9 (1.4, 8.1)	1.4**

HR, hazard ratio; NE (not estimable) indicates that the response was not reached within the 12-week period. ***p<0.001

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Results: Pts had a disease duration of 7 and 13 years in NEXT and BEYOND respectively.^{1,2} In BEYOND, pts were treatment-refractory as evidenced by 53% having received ≥2 prior bDMARDs². Median times to achieve ACR20 were similar, irrespective of pt population, being 4 wks for UPA 15 mg QD and 2–3 wks for

UPA 30 mg QD vs 12 wks on PBO (p<0.001). In general, the median times to achieve ACR50 and DAS28-CRP≤3.2 for UPA 15 mg and 30 mg QD were ~12 wks and ~8 wks for both csDMARD-IR and bDMARD-IR pts, whereas the median was not reached for pts on PBO during the first 12 wks (p<0.001, table 1). The median time to LDA by CDAI and SDAI was ~12 wks across UPA doses and populations, but was not reached for pts receiving PBO within that time. Pts receiving UPA were 2–4 times more likely to achieve clinical responses vs pts receiving PBO. In general, both UPA doses performed similarly across pt populations, with numerically quicker responses observed in pts receiving UPA 30 mg vs UPA 15 mg QD. Median times to achieve 20% and 50% improvements in tender and swollen joint counts were 1–2 wks and 2–4 wks respectively, for both UPA doses, irrespective of pt population. Median times to achieve 20% improvements in morning stiffness duration and severity were approximately 2 wks in each of the UPA arms vs 4 wks on PBO (p<0.001).

Conclusions: Pts receiving UPA at either 15 mg or 30 mg QD were more likely to achieve clinical responses at significantly earlier time points when compared with pts receiving PBO. Irrespective of being csDMARD-IR or bDMARD-IR, times to achieve various clinical responses were consistent between pt populations.

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SAT0240

VAGUS NERVE STIMULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: TWO-YEAR SAFETY AND EFFICACY

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Background: Rheumatoid arthritis (RA) is a debilitating chronic disease with an unmet need for additional therapeutic approaches. Activating neuro-immune reflex pathways by stimulation of the vagus nerve (VNS) could represent a novel means of treating RA [1] and other immune-mediated inflammatory diseases. Last year we reported a 12-week proof-of-concept study using a VNS device, approved for drug-resistant epilepsy, showing reduction in the DAS28-CRP clinical disease activity score, with concomitant reductions in TNF and IL-6 levels [2].

Objectives: To understand the long term safety and efficacy of this novel treatment approach, we followed the patients in a 24 months long-term extension study and report on the safety and clinical efficacy data.

Methods: VNS devices were implanted into 17 RA patients, mostly with insufficient response to multiple conventional and biologic disease-modifying antirheumatic drugs (DMARDs), on stable background of methotrexate (≤25 mg weekly) therapy. The devices electrically stimulated the vagus nerve, 1–4 min/day, over a 12 week open label period. On completion, subjects were offered to enroll into a follow-up study, where the study physicians were given flexibility to alter VNS dosing parameters and/or to add a biologic DMARD to the treatment regimen. DAS28-CRP and Health Assessment Questionnaire-Disability Index (HAQ-DI) were collected over 2 years.

Results: All subjects electively continued on VNS treatment through 24 months of the long term follow-up study. Biologic DMARDs were started in 1 and restarted in 8 of 17 subjects; of these, 4 were non-responders to VNS, and 5 had stable improvement but had not yet achieved disease remission on VNS alone (table 1). At the start of the follow-up study, the mean DAS28–28 and HAQ-DI were significantly reduced compared to the pre-implant baseline (mean difference±SE in DAS28-CRP=–1.60±0.37, p<0.0001; mean difference±SE in HAQ-DI = –0.44±0.21, p<0.037), and the depth of effect was retained through 24 months. At 24 months, there was no significant difference in DAS28-CRP between the subjects using VNS monotherapy or those using a combination of VNS and biologic