and Δ HAQ-DI are presented. The area under the curve (AUC) was calculated for ACR-n up to Month 12 (in months), and an analysis of covariance model was used to assess treatment effects in terms of the AUC of ACR-n at Month 12; there was no adjustment for multiplicity for this post hoc analysis.

Results: The cumulative probability plots of ACR responses at Month 12 indicated that the proportion of patients who achieved responses of ACR20, ACR50 and ACR70 was similar for tofacitinib + MTX and adalimumab + MTX, but was numerically smaller for tofacitinib monotherapy (figure, A). Responses of approximately $\geq$ ACR80 were achieved by a similar proportion of patients in each treatment group. Least squares mean (standard error) AUC of ACR-n up to Month 12 (in months) was similar for tofacitinib + MTX (437 [35]) and adalimumab + MTX (402 [35]), but was smaller for tofacitinib monotherapy (319 [35]; $p < 0.05$). The cumulative probability plots of Δ HAQ-DI suggested that, in general, reductions from baseline in HAQ-DI were similar across treatment groups (figure, B), although a slightly higher proportion of patients who received tofacitinib monotherapy reported an increase in HAQ-DI vs other treatments.

ACR-n, American College of Rheumatology response, where n represents the minimum % response achieved by each patient; BID, twice daily; Δ HAQ-DI, change from baseline in Health Assessment Questionnaire-Disability Index; MTX, methotrexate; Q2W, once every 2 weeks; SC, subcutaneous

Figure 1 Cumulative probability plot of A) ACR response and B) Δ HAQ-DI at Month 12. Two outliers for ACR response are not shown: tofacitinib 5 mg BID monotherapy, ACR-n=1700, cumulative probability=0.0003; adalimumab 40 mg SC Q2W + MTX, ACR-n=463, cumulative probability=0.003

Conclusions: These data support the primary ORAL Strategy findings,¹ indicating that in patients with RA, clinical efficacy, based on ACR response, was generally similar for tofacitinib + MTX and adalimumab + MTX, while a smaller proportion of patients who received tofacitinib monotherapy achieved ACR response in general, and particularly for $<$ ACR80. Functional efficacy, based on Δ HAQ-DI, was generally similar across all treatment groups. Cumulative probability analyses for CDAI will be further evaluated.

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SAT0253 DOSE REDUCTION OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING SUSTAINED DISEASE CONTROL: RESULTS OF A PROSPECTIVE STUDY

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Background: In patients with rheumatoid arthritis (RA) and inadequate response (IR) to DMARDs, ph3 studies demonstrated efficacy of baricitinib (Bari) (2-mg and 4-mg).

Objectives: To investigate the effects of Bari dose step-down in patients who achieved sustained disease control with Bari 4-mg.

Methods: Patients with RA participating in the Bari ph3 long-term extension study who received Bari 4-mg for ≥ 15 months and who achieved sustained low disease activity (LDA) – CDAI score ≤ 10 or remission (REM) – CDAI ≤ 2.8 ≥ 3 months apart were re-randomised in a blinded manner to continue Bari 4-mg or step down to 2-mg. Patients could rescue to Bari 4-mg. Efficacy and safety were assessed through 48 weeks (wks) following re-randomisation.

	Patients Originating from RA-BEAM, RA-BUILD, RA-BEACON Combined [†]					
	Wk 12		Wk 24		Wk 48	
	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376
Efficacy measure	NRI after rescue or for missing data					
CDAI LDA ≤10	338/374 (90.4)	310/376 (82.4)**	327/374 (87.4)	280/376 (74.5)***	300/374 (80.2)	254/376 (67.6)***
CDAI REM ≤2.8	149/374 (39.8)	134/376 (35.6)	161/374 (43.0)	130/376 (34.6)*	145/374 (38.8)	121/376 (32.2)
	NRI only for missing data (observed data used after rescue)					
CDAI LDA ≤10	338/374 (90.4)	310/376 (82.4)**	334/374 (89.3)	304/376 (80.9)**	321/374 (85.8)	295/376 (78.5)**
CDAI REM ≤2.8	149/374 (39.8)	134/376 (35.6)	164/374 (43.9)	137/376 (36.4)*	149/374 (39.8)	134/376 (35.6)
Safety measure	Wks 0–48					
n [EAIR]	Continued Bari 4-mg N=374			Stepped down to Bari 2-mg N=376		
SDEAE	235 [69.30]			202 [63.46]		
Infection	108 [31.85]			78 [24.50]		
SAE	27 [7.96]			26 [8.17]		
Serious infection	10 [2.95]			4 [1.26]		
AE	9 [2.64]			12 [3.74]		
→discontinuation						

Efficacy and safety data are n/N (%), and n [EAIR], respectively. [†]RA-BEAM=MTX-IR patients; RA-BUILD=csDMARD-IR patients; RA-BEACON=bDMARD-IR patients; EAIR=exposure-adjusted incidence rate; NRI=nonresponder imputation; SDEAE=step-down emergent adverse event; * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ vs. continued Bari 4-mg

Figure 1. Data represent patients who have completed 48 weeks in the step-down period, or would have completed 48 weeks if not discontinued prior to the data cut-off date (April 1, 2017). Relapse defined as loss of step-down eligibility criteria, CDAI >10 for patients originating from RA-BUILD, RA-BEAM, or RA-BEACON. The p-value was computed using the Wilcoxon test.

Results: The majority of patients in both groups maintained the state of LDA or REM over the 48 wks. However, dose reduction to 2-mg resulted in significant increases in disease activity at 12, 24, and 48 wks (Table). Dose reduction also resulted in a shorter time to relapse (defined as loss of step-down eligibility criteria); significantly more patients relapsed over 48 wks compared to the 4-mg group (figure 1). Rescue rates were 8.3% for Bari 4-mg, 16.6% for Bari 2-mg. Most rescued patients could regain LDA or REM. Dose reduction was associated with a lower rate of infections; rates of SAEs and AEs leading to discontinuation were similar across groups.

Conclusions: These data indicate that disease control was better maintained with Bari 4-mg than 2-mg. However, most stepped-down patients could maintain LDA or REM, or recapture control with re-introduction of the 4-mg dose. Stepping down to a dose of 2-mg daily may be a viable option for many patients who have achieved sustained LDA or REM on the 4-mg dose.

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SAT0254

UPADACITINIB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: RESULTS FROM SELECT-NEXT

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Background: Upadacitinib (UPA), a selective JAK-1 inhibitor, has demonstrated efficacy in active RA among patients with an inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD-IR).¹ To understand treatment effectiveness from the patients' perspective we examined the impact of UPA on patient-reported outcomes (PROs).

Objectives: To evaluate the effect of UPA vs placebo (PBO) on PROs in SELECT-NEXT (NCT02675426), a randomized controlled trial assessing the efficacy and safety of UPA in csDMARD-IR RA patients.

Methods: Patients in SELECT-NEXT received UPA 15 mg or 30 mg daily or PBO for 12 weeks followed by a 5-year extension phase. PROs included physical function (Health Assessment Questionnaire Disability Index [HAQ-DI]), Patient's Global Assessment of Disease Activity (PtGA) by visual analog scale (VAS), pain by VAS, fatigue by FACIT-F, duration and severity of morning (AM) stiffness, quality of life (QoL) by Short Form 36 Health Survey [SF-36], and Work Instability Scale for RA (RA-WIS). Changes in least square means (LSMs) from baseline (BL) to week 12 were based on mixed effect repeated measures models. Percentages of patients reporting changes in PRO scores from BL to week 12 $\geq$ minimum clinically important differences (MCIDs) or scores $\geq$ normative values (age- and gender-matched for SF-36 only) were determined for UPA and PBO arms; comparisons between groups used chi-square tests. For each PRO, the incremental number needed to treat (NNT) to achieve clinically meaningful improvement from BL ($\geq$ MCID) was calculated.

Results: Data from 661 patients (221 in UPA 15 mg; 219 in UPA 30 mg; 221 in PBO) were analysed. Mean age was 56 years, 79% were female; 45% had RA for $\geq$ 5 years. Statistically significant LSM changes from BL to week 12 were reported with both UPA doses vs PBO for HAQ-DI, PtGA, pain, FACIT-F, duration and severity of AM stiffness, SF-36 (PCS; 6 or 7/8 domains), and RA-WIS (Table). Compared with PBO at week 12, significantly more UPA-treated (both doses) patients reported improvement $\geq$ MCID in HAQ-DI, PtGA, pain, FACIT-F, duration and severity of AM stiffness, SF-36 (PCS; 4 or 7/8 domains), and RA-WIS as well as scores $\geq$ normative values in HAQ-DI, PtGA, FACIT-F, SF-36 (PCS; 4 or 5/8 domains). For most PROs, NNTs with UPA ranged from 4 to 8 patients.

Table 1 LSM changes from baseline and percentage of responders at week 12 after UPA initiation

PRO	Change from Baseline			% Responders					
	LSM			Reporting Scores $\geq$ MCID, n (%)			Reporting Scores $\geq$ Normative Values, n (%)		
	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219	PBO N=221	UPA 15 mg N=221	UPA 30 mg N=219
HAQ-DI	-0.26	-0.61*	-0.55*	109 (49.3)	156 (70.2)*	148 (67.6)*	30 (13.6)	56 (25.9)*	54 (24.7)*
PtGA	-10.36	-29.67*	-30.51*	94 (42.5)	153 (70.5)*	158 (72.1)*	32 (14.5)	78 (35.9)*	84 (38.4)*
Pain VAS	-10.26	-29.92*	-31.71*	97 (43.9)	158 (72.8)*	160 (73.1)*	—	—	—
FACIT-F	2.96	7.91*	7.74*	91 (41.2)	138 (63.9)*	123 (56.7)*	35 (15.8)	60 (27.8)*	66 (30.4)*
Duration AM stiffness*	-34.27	-85.28*	-85.13*	29 (13.4)	57 (26.3)* ^b	57 (26.5)* ^b	—	—	—
Severity AM stiffness*	-1.38	-2.88*	-3.26*	130 (60.2)	165 (76.0)* ^b	172 (80.4)* ^b	—	—	—
SF-36 PCS	3.03	7.58*	8.01*	106 (48.0)	152 (69.4)*	151 (69.6)*	18 (8.1)	39 (17.8)*	33 (15.2)*
SF-36 MCS	2.58	4.69*	3.67	91 (41.2)	120 (54.8)*	98 (45.2)	102 (46.2)	114 (52.1)	108 (49.8)
SF-36 PF	2.96	6.92*	6.81*	126 (57.0)	175 (79.2)*	143 (65.3)	26 (11.8)	52 (23.5)*	53 (24.2)*
SF-36 RP	2.88	6.40*	6.36*	115 (52.0)	156 (70.6)*	141 (64.4)*	18 (8.1)	39 (17.6)*	44 (20.1)*
SF-36 BP	4.66	9.44*	10.38*	123 (55.7)	162 (73.3)*	163 (74.4)*	39 (17.6)	75 (33.9)*	71 (32.4)*
SF-36 GH	1.92	5.61*	5.00*	112 (50.7)	143 (64.7)*	141 (64.4)*	35 (15.8)	51 (23.1)	54 (24.7)*
SF-36 VT	2.52	6.77*	7.05*	104 (47.1)	148 (67.0)*	141 (64.4)*	56 (25.3)	85 (38.5)*	88 (40.6)*
SF-36 SF	2.53	6.17*	4.81*	99 (44.8)	125 (56.6)*	112 (51.1)	67 (30.3)	81 (36.7)	85 (38.8)
SF-36 RE	2.62	5.59*	4.10	85 (38.5)	112 (50.7)*	104 (47.5)	75 (33.9)	88 (39.8)	89 (40.6)
SF-36 MH	3.39	4.78	4.77	121 (54.8)	135 (61.1)	115 (52.5)	75 (33.9)	83 (37.6)	87 (39.7)
RA-WIS	-1.55	-4.28*	-3.48*	17 (7.5)	44 (44.4)*	29 (31.9)*	43 (44.3)	56 (56.6)	41 (45.1)

*P<0.05 for UPA vs PBO.

^aDuration in minutes. ^b% responders reporting scores $\geq$ minimal important difference. ^cAssessed on a numeric scale of 1-10, 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.

Conclusions: Treatment with UPA 15 mg or 30 mg daily for 12 weeks resulted in significant and clinically meaningful improvements in physical function, pain, fatigue, AM stiffness, QoL, and less work instability among csDMARD-IR RA patients. The NNTs to achieve these improvements were favourable.