PYs, respectively. Starting from Wk26, background csDMARDs were initiated for approximately 18% of pts.

Based on As Observed data, for pts on UPA from BL through Wk48 on UPA15 [250/300 (83%)] and UPA30 [251/298 (84%)], clinical and functional outcomes continued to improve, or were maintained (Table 1). For pts continuing UPA15 and 30, DAS28-CRP<2.6 was 55% and 68%, and CDAI≤2.8 was 28% and 42%, respectively. Pts who were switched from cMTX to UPA15 or 30 at Wk14 had similar responses at Wk 48.

The most frequently reported treatment-emergent AEs were urinary tract infection, blood creatine phosphokinase increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, herpes zoster (HZ), alanine aminotransferase increase, and bronchitis. The most frequently reported serious AE was pneumonia (8 events). Events/100PYs were numerically higher in the UPA30 vs UPA15 arm for HZ, and hepatic disorders, and were comparable for serious infections and malignancies excluding non-melanoma skin cancer (Table 2). Adjudicated venous thromboembolic events (VTE) were observed only on UPA15 (2 pts with deep vein thrombosis and 2 pts with pulmonary embolism; all patients had at least one risk factor for VTE).

Conclusion: UPA 15 or 30 monotherapy resulted in similar improvements in signs and symptoms and physical function through 48 wks. The overall benefit-risk profile of both doses of UPA was favorable based on safety and efficacy data through Wk48 but will be confirmed through an integrated safety analysis across all the ph 3 trials.

Abstract THU0191 –Table 1.

	cMTX → UPA 15 MG	cMTX → UPA 30 MG	UPA 15 MG	UPA 30 MG
ACR20	77/96 (80)	75/91 (82)	150/172 (87)	162/186 (87)
ACR50	63/94 (67)	55/92 (60)	122/174 (70)	133/185 (72)
ACR70	44/94 (47)	39/93 (42)	80/176 (46)	99/183 (54)
DAS28-CRP<2.6	67/96 (70)	66/92 (72)	126/174 (72)	148/185 (80)
DAS28-CRP<2.6	56/96 (58)	50/92 (54)	96/174 (55)	128/185 (68)
CDAI≤30	68/95 (72)	65/90 (72)	123/172 (72)	143/185 (77)
CDAI≤2.8	26/95 (27)	19/90 (21)	48/172 (28)	77/185 (42)
Change from BL in HAQ-DI	-0.69	-0.73	-0.73	-0.83

Abstract THU0191 –Table 2.

	UPA 15 MG N=318 PYs=336.0 E/100PYs	UPA 30 MG N=311 PYs=337.1 E/100PYs
Any Adverse Event	254.2	319.2
Serious AE	19.6	17.8
AE Leading To Discontinuation Of Study Drug	8.9	10.1
Serious Infection [§]	5.1	4.4
Herpes Zoster [†]	3.3	7.7
Hepatic disorder [‡]	7.7	12.5
Any Malignancy (excluding NMSC) [¶]	1.5	1.2
MACE (adjudicated) [§]	0.9	1.5
Venous Thromboembolism (adjudicated)	1.2	0
Death [*]	0.9	0.3
E/100PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular (CV) event (CV death, non-fatal myocardial infarction [MI], non-fatal stroke)		
[§] Serious Infection: Most frequently reported SI were pneumonia, bronchitis, cellulitis, HZ and UTI		
[†] Herpes zoster: mostly 1 or 2 dermatomes, 1 ophthalmic		
[‡] Hepatic disorder: mostly transaminase elevations that were mild to moderate in severity.		
[¶] Malignancies: 5 breast cancers (UPA15: 3 pts, UPA30: 2 pts), 2 colorectal cancers (UPA15: 1 pt, UPA30: 1 pt), 1 non-Hodgkin's lymphoma (UPA15), 1 malignant melanoma (UPA30)		
[§] MACE : UPA15: 3 CV deaths; UPA 30: 2 non-fatal MI, 2 non-fatal stroke; 1 CV death		
[*] Deaths: UPA15: 1 hemorrhagic stroke (ruptured aneurysm), 1 congestive cardiomyopathy and 1 sudden cardiac death; UPA30: 1 fatal MI.		

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THU0192 UPADACITINIB MONOTHERAPY IMPROVES PATIENT-REPORTED OUTCOMES IN METHOTREXATE-NAÏVE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM SELECT-EARLY

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Background: Monotherapy use of upadacitinib (UPA), a selective JAK1 inhibitor, demonstrated clinically meaningful improvement in the signs and symptoms of rheumatoid arthritis (RA) compared with methotrexate (MTX).¹ To better understand the impact of UPA treatment in RA from the patient's perspective, we examined the effect of UPA on patient-reported outcomes (PROs).

Objectives: To evaluate the effect of UPA monotherapy vs MTX at week 12 on PROs in SELECT-EARLY (NCT02706873), a randomised controlled trial in MTX-naïve patients with moderate to severe RA.

Methods: Patients were randomised 1:1:1 to receive once daily UPA (15 mg or 30 mg) or weekly MTX (titrated by Week 8). PROs assessed included Patient Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), pain by VAS, physical function by Health Assessment Questionnaire Disability Index (HAQ-DI), fatigue by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration and severity of morning (AM) stiffness, HRQoL by Short Form 36 (SF-36), and Work Productivity and Activity Impairment (WPAI) measure. Least square mean (LSM) changes from baseline (BL) to Week 12 were based on analysis of covariance. Percentages of patients reporting changes in PRO scores from BL to Week 12 ≥ minimum clinically important differences (MCIDs) or scores ≥ normative values (age- and gender-matched for SF-36 only) were determined for UPA and MTX groups; comparisons used chi-square tests. For each PRO, the incremental number needed to treat (NNT) to achieve clinically meaningful improvement from BL was calculated.

Results: Data from 945 patients (MTX: 314; UPA 15 mg: 317; UPA 30 mg: 314) were analysed. Mean age was 53 years; 76% were female; 49% had RA for <6 months. Statistically significant LSM changes from BL to Week 12 were reported for both doses of UPA vs MTX for all PROs (Table). At Week 2, both UPA doses had significantly higher proportions of patients reporting improvements ≥ MCID vs MTX in HAQ-DI, duration and severity of AM stiffness, pain, and PtGA. Compared with MTX at Week 12, a significantly greater proportion of patients receiving UPA at either dose reported improvements ≥ MCID in all PROs. A significantly greater proportion of patients receiving UPA also reported scores ≥ normative values for all PROs except SF-36 Mental Health (UPA 15 mg) and SF-36 General Health (both UPA doses) domains. For most PROs, NNTs with UPA ranged from 4 to 8 patients at Week 12.

Abstract THU0192 –Table 1.

PRO	Baseline Mean	LSM Changes From Baseline			Patients Reporting Improvements ≥MCI, n (%)		
	(n=945)	MTX (n=314)	UPA 15 mg (n=317)	UPA 30 mg (n=314)	MTX (n=314)	UPA 15 mg (n=317)	UPA 30 mg (n=314)
PtGA	65.8	-24.6	-34.9*	-38.0*	190 (60.5)	248 (78.2)*	230 (74.0)*
Pain VAS	66.5	-25.4	-36.3*	-39.7*	195 (62.1)	249 (78.5)*	241 (77.5)*
HAQ-DI	1.6	-0.5	-0.8*	-0.9*	189 (60.2)	248 (78.2)*	247 (79.4)*
FACT-F	26.9	6.8	10.0*	9.6*	171 (54.5)	207 (65.5)*	203 (65.5)*
Duration AM stiffness ^a	144.7	-72.4	-106.0*	-111.5*	72 (23.0) ^b	120 (38.0)* ^b	115 (36.7)* ^b
Severity AM stiffness ^c	6.5	-3.0	-4.0*	-4.1*	222 (70.9) ^b	262 (82.9)* ^b	262 (83.7)* ^b
SF-36 PCS	33.2	5.8	10.1*	10.1*	182 (58.0)	250 (79.1)*	245 (78.5)*
SF-36 MCS	43.0	3.9	5.8*	5.8*	139 (44.3)	187 (59.2)*	165 (52.9)*
SF-36 PF	32.2	5.6	10.0*	10.1*	205 (65.3)	253 (80.1)*	245 (78.0)*
SF-36 RP	34.0	4.7	8.4*	8.6*	164 (52.2)	232 (73.4)*	221 (70.4)*
SF-36 BP	33.8	7.4	11.9*	11.9*	194 (61.8)	262 (82.9)*	249 (79.3)*
SF-36 GH	39.8	4.4	6.3*	6.8*	174 (55.4)	214 (67.7)*	219 (69.7)*
SF-36 VT	40.8	5.5	9.3*	8.6*	183 (58.3)	242 (76.6)*	221 (70.4)*
SF-36 SF	38.3	4.6	7.7*	8.1*	155 (49.4)	199 (63.0)*	195 (62.1)*
SF-36 RE	38.2	4.2	6.4*	6.8*	138 (43.9)	188 (59.5)*	176 (56.1)*
SF-36 MH	41.0	4.6	6.9*	6.8*	160 (51.0)	214 (67.7)*	200 (63.7)*
WPAI Work Impairment ^d	56.3	-9.8	-26.6*	-23.5*	47 (35.9)	87 (61.3)*	66 (55.0)*
WPAI Activity Impairment	62.8	-19.0	-27.6*	-31.2*	183 (58.3)	231 (73.3)*	233 (75.2)*

*P<0.05 for UPA vs MTX.

^a Duration in minutes. ^b % responders reporting scores ≥minimal important difference. ^c Assessed on a numeric scale of 1–10, with 10 being the worst level. ^d Calculated only for employed patients.

AM, morning; BP, bodily pain; Functional Assessment of Chronic Illness Therapy–Fatigue (FACT-F); GH, general health; HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MCI, minimum clinically important difference; MCS, Mental Component Summary; MH, mental health; MTX, methotrexate; PCS, Physical Component Summary; PF, physical function; PRO, patient-reported outcome; PGA, Patient Global Assessment of Disease Activity; RE, role emotional; RP, role physical; SF, social function; SF-36, 36-Item Short Form Health Survey; UPA, upadacitinib; VAS, visual analogue scale; VT, vitality; WPAI, Work Productivity and Activity Impairment questionnaire.

Conclusion: Among MTX-naïve patients with active RA, treatment with UPA 15 mg or 30 mg daily for 12 weeks resulted in statistically significant and clinically meaningful improvements in physical function, pain, fatigue, AM stiffness, HRQoL, and work productivity compared with MTX. The NNTs to achieve these improvements were favourable.

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THU0193

EFFICACY OF TOFACITINIB MONOTHERAPY, TOFACITINIB WITH METHOTREXATE AND ADALIMUMAB WITH METHOTREXATE IN PATIENTS WITH EARLY (≤2 YEARS) VS ESTABLISHED (>2 YEARS) RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM ORAL STRATEGY

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Greater improvements in efficacy outcomes have been reported with tofacitinib 5 mg BID ± csDMARDs in patients (pts) with early vs established RA.^{1,2}

Objectives: This post hoc analysis of ORAL Strategy data evaluated the efficacy and safety of tofacitinib monotherapy, tofacitinib + methotrexate (MTX) and adalimumab (ADA) + MTX, stratified by baseline (BL) RA duration.

Methods: ORAL Strategy (NCT02187055) was a P3b/4, 1-yr, double-blind, triple-dummy, active comparator-controlled study. MTX inadequate-responder pts were randomised 1:1:1 to receive tofacitinib 5 mg BID (tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX), or ADA SC 40 mg Q2W + MTX (ADA+MTX); MTX was dosed at 15–25 mg/wk except in cases of intolerance/toxicity. In this analysis, pts were stratified by BL RA duration as having early (≤2 yrs) or established (>2 yrs) RA. Efficacy outcomes (Months [M]3, 6 and 12): ACR20/50/70; change from BL (Δ) in DAS28-4(ESR), SDAI and CDAI; and rates of DAS28-4(ESR), SDAI and CDAI-defined LDA (≤3.2, ≤11 and ≤10, respectively) and remission (<2.6, ≤3.3 and ≤2.8, respectively). Nominal p values for treatment comparisons were calculated without multiplicity adjustment; p<0.05 was considered significant. Treatment-emergent AEs and serious AEs (SAEs) were assessed throughout the study.

Table: Demographics and disease characteristics at baseline, and safety up to Month 12

	Early RA (≤2 years)			Established RA (>2 years)		
	Tofacitinib monotherapy N=80	Tofacitinib + MTX N=83	Adalimumab + MTX N=78	Tofacitinib monotherapy N=304	Tofacitinib + MTX N=293	Adalimumab + MTX N=308
Baseline demographics and disease characteristics^a						
Age (years), mean (SD)	47.1 (12.9)	46.2 (13.8)	48.2 (13.5)	50.4 (12.0)	51.0 (13.1)	51.0 (13.3)
Female, n (%)	66 (82.5)	69 (83.1)	60 (76.9)	253 (83.2)	242 (82.6)	260 (84.4)
RA duration (years), mean (SD)	1.0 (0.5)	1.1 (0.5)	1.0 (0.5)	10.4 (7.7)	9.4 (8.9)	10.0 (7.1)
DAS28-4(ESR), mean (SD)	6.6 (0.8)	6.4 (0.8)	6.4 (1.0)	6.5 (0.9)	6.6 (0.9)	6.5 (1.0)
SDAI, mean (SD)	41.9 (12.6)	38.9 (11.1)	39.9 (12.9)	39.8 (13.1)	42.4 (13.6)	39.8 (13.5)
CDAI, mean (SD)	40.0 (12.2)	37.2 (10.9)	38.2 (12.4)	38.2 (12.6)	40.5 (13.1)	38.2 (13.0)
HAQ-DI, mean (SD)	1.6 (0.6)	1.4 (0.6)	1.5 (0.6)	1.6 (0.6)	1.6 (0.6)	1.6 (0.6)
RF+, n (%)	45 (56.3)	42 (50.6)	47 (60.3)	214 (70.4)	203 (69.5)	212 (69.3)
Anti-CCP+, n (%)	59 (73.8)	56 (67.5)	52 (66.7)	232 (76.3)	223 (76.1)	246 (79.9)
Prior medications						
TNFi, n (%)	2 (2.5)	1 (1.2)	0	26 (8.6)	15 (5.1)	19 (6.2)
Non-TNFi, n (%)	1 (1.3)	1 (1.2)	0	19 (6.9)	13 (4.4)	20 (6.5)
MTX dose (mg/wk)	16.4 (3.2)	17.1 (3.1)	16.9 (3.7)	16.8 (3.3)	16.5 (3.9)	16.3 (3.7)
GC use, n (%)	50 (62.5)	47 (56.6)	39 (50.0)	178 (58.6)	168 (57.3)	184 (59.7)
GC dose (mg/day), mean (SD)	7.0 (3.1)	6.6 (2.4)	6.5 (3.5)	7.7 (3.5)	6.4 (2.6)	6.4 (2.4)
Safety						
AE	52 (65.0)	47 (56.6)	53 (67.9)	174 (57.2)	184 (62.8)	200 (64.9)
SAE	10 (12.5)	2 (2.4)	8 (10.3)	25 (8.2)	24 (8.2)	16 (5.2)

N for each assessment may differ from N for each treatment group. ^aAverage dose immediately prior to randomisation.

AE, adverse event; Anti-CCP, anti-cyclic citrullinated peptide antibody; CDAI, Clinical Disease Activity Index; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire-Disability Index;

MTX, methotrexate; RA, rheumatoid arthritis; RF, rheumatoid factor; SDAI, Simplified Disease Activity Index;

SD, standard deviation; TNFi, tumour necrosis factor inhibitor; wk, week.

Figure: ACR50 response rates and ΔDAS28-4(ESR) up to Month 12 (FAS)

^aUsing non-responder imputation

^bp<0.05, ^cp<0.001, ^dp<0.0001 tofacitinib monotherapy vs tofacitinib + MTX; ^ep<0.05 tofacitinib monotherapy vs adalimumab + MTX;

^fp<0.05 tofacitinib + MTX vs adalimumab + MTX

Δ, change from baseline; ACR, American College of Rheumatology; DAS28-4(ESR), Disease Activity Score in 28 joints based on erythrocyte sedimentation rate; FAS, full analysis set; LS, least squares; MTX, methotrexate; RA, rheumatoid arthritis; SE, standard error

Abstract THU0193 – Figure 1