Table 1. Proportion of patients maintaining Week 26 CDAI and DAS28(CRP) responses during 6-month follow-up by initial therapy with UPA or ADA in SELECT-COMPARE^{a,c}

	UPA 15 mg QD	ADA 40 mg EOW
CDAI LDA (≤ 10)	43.9	36.3
CDAI Remission (≤ 2.8)	35.0	22.7
DAS28(CRP) ≤ 3.2	39.1	35.3
DAS28(CRP) < 2.6	30.5	30.1

^aAs observed.^bBlinded rescue from UPA to ADA or ADA to UPA was permitted at Week 14, 18, and 22 for patients with $< 20\%$ improvement in TJC or SJC and at Week 26 for patients with a CDAI < 10 . Data are presented and attributed to original randomized group (UPA or ADA) regardless of any subsequent switch in therapy.^cMaintaining response defined as never losing response at any visit during ~6 months (22–26 weeks) follow up after first achieving response before or at Week 26.

ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; EOW, every other week; QD, once daily; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib.

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POS0654

IMPACT OF CONCOMITANT GLUCOCORTICOIDS ON THE CLINICAL EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN AD HOC ANALYSIS OF DATA FROM THREE PHASE 3 STUDIES

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Background: Glucocorticoid (GC) therapy has strong anti-inflammatory effects and helps slow radiographic progression in RA¹; however, GCs can be associated

with adverse events (AEs) such as infection, especially with long-term use and higher doses.

Objectives: To evaluate the impact of baseline GCs on the efficacy and safety of upadacitinib (UPA) with or without concomitant conventional synthetic DMARDs (csDMARDs).

Methods: In this ad hoc analysis of three Phase 3 studies, patients with inadequate response to MTX (MTX-IR) receiving UPA 15 mg once daily (QD) or placebo (PBO) + csDMARDs in SELECT-NEXT, and MTX-IR/MTX-naïve patients receiving UPA 15 mg QD monotherapy or MTX monotherapy in SELECT-MONOTHERAPY/SELECT-EARLY, respectively, were included. Efficacy outcomes, including measures of remission and low disease activity (LDA) determined by DAS in 28 joints using CRP (DAS28[CRP]; $< 2.6/\leq 3.2$) and Clinical Disease Activity Index (CDAI; $\leq 2.8/\leq 10$), were assessed and stratified by baseline GC use. Patients were permitted to receive oral GCs ≤ 10 mg/day (prednisone equivalent) at baseline with no adjustment permitted until Week 24/26/48. Safety was reported as number and proportion of patients with AEs. Data were analyzed descriptively with no statistical comparisons between groups or doses.

Results: Of 1,506 patients included in the analysis, 737 (48.9%) were receiving baseline GCs (mean dose 6.2 mg/day). Baseline characteristics were broadly similar across treatment groups; SELECT-EARLY, which enrolled MTX-naïve patients, generally had the shortest duration of RA and higher CRP levels. Across UPA treatment groups, concomitant GCs generally did not influence the proportions of patients achieving remission (Figure 1). In SELECT-NEXT, clinical responses with UPA 15 mg in combination with csDMARDs were similar irrespective of concomitant GC use (Figure 1). Within SELECT-MONOTHERAPY, responses in patients receiving UPA 15 mg without concomitant csDMARDs or GCs were higher than those in patients receiving MTX alone, but were numerically lower than in those receiving UPA 15 mg with GCs (Figure 1). However, this was not observed within SELECT-EARLY, where clinical responses in patients receiving UPA 15 mg monotherapy without GCs were higher than in those patients receiving UPA 15 mg with GCs for both DAS28(CRP) < 2.6 (40.6% vs 29.9%, respectively) and CDAI ≤ 2.8 (20.0% vs 11.6%, respectively) (Figure 1). A similar trend was observed for LDA. Serious AEs, AEs leading to discontinuation, and AEs of special interest, including infections (such as herpes zoster), were broadly similar in the UPA groups irrespective of concomitant GC use (**table of safety data will be presented**).

Conclusion: UPA 15 mg in combination with csDMARDs or as monotherapy was effective in achieving remission and LDA, irrespective of concomitant GC use. Safety of UPA, including incidence of infection, appeared largely unaffected by concomitant GC use.

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Figure. Efficacy in patients receiving UPA or PBO with/without csDMARDs, and with/without GCs^a

^aNon-responder imputation.

CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; DAS28(CRP), Disease Activity Score in 28 joints using CRP; GC, glucocorticoid; PBO, placebo; QD, once daily; UPA, upadacitinib.

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POS0655

LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 3-YEAR RESULTS FROM THE SELECT-EARLY STUDY

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Background: Upadacitinib (UPA), an oral Janus kinase inhibitor, demonstrated significant improvements in signs, symptoms, and structural inhibition as monotherapy (mono) vs methotrexate (MTX) in MTX-naïve patients (pts) with rheumatoid arthritis (RA) through 48 weeks (wks).¹

Objectives: To report the efficacy and safety of UPA vs MTX mono up to 156 wks in pts with RA from the ongoing long-term extension (LTE) of the SELECT-EARLY trial.

Methods: During the 48-wk double-blind study period, pts were randomized to UPA 15 or 30 mg once daily (QD) or MTX (titrated to 20 mg/wk by Wk 8). At Wk 26, pts who did not achieve Clinical Disease Activity Index (CDAI) remission (≤ 2.8) and had $<20\%$ improvement from baseline in tender or swollen joint count received blinded rescue therapy (addition of MTX for UPA groups and UPA 15 or 30 mg for MTX group). In the LTE, pts received open-label treatment once the last pt reached Wk 48. Efficacy assessments up to Wk 156 were summarized by randomized group and included American College of Rheumatology (ACR) responses, remission and low disease activity (LDA) measures, and change in modified Total Sharp Score (mTSS; up to 96 wks). Treatment-emergent adverse events (AEs) per 100 pt-years (PY) for pts on continuous mono were summarized through 156 wks. Non-responder imputation was used for binary endpoints for missing data and when pts received rescue therapy or prematurely discontinued the study drug.

Results: Of 945 pts randomized and treated, 775 entered the LTE on study drug (including 57 rescued pts; MTX, 33; UPA 15 mg, 17; UPA 30 mg, 7). Overall, 161 (21%) pts discontinued during the LTE. At Wk 156, higher proportions of pts randomized to UPA achieved a 20/50/70% improvement in ACR response (ACR20/50/70), LDA, and remission vs MTX (Figure 1). Change from baseline in mTSS at Wk 96 favored UPA vs MTX (data not shown). Most AEs were numerically more frequent with UPA 30 mg. The overall rate of serious infection was numerically higher with UPA vs MTX (Table 1). Herpes zoster (HZ), neutropenia, non-melanoma skin cancer (NMSC), and creatine phosphokinase (CPK) elevation were more frequent with UPA vs MTX. Two active tuberculosis (TB) events were reported in each UPA arm; 3 adjudicated gastrointestinal (GI) perforation events were observed in the UPA 30 mg arm. Adjudicated major adverse cardiovascular events (MACEs) or venous thromboembolic events (VTEs) were comparable across treatment arms.

Conclusion: UPA monotherapy showed sustained clinically meaningful responses including remission vs MTX through Wk 156 but higher rates of several AEs, including HZ, neutropenia, and CPK elevations; no new safety risks were observed compared with previous results.^{1,2}

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Table 1. Safety overview

E/100 PY (95% CI)	MTX mono (n=314; PY=601.9)	UPA 15 mg QD mono (n=317; PY=703.4)	UPA 30 mg QD mono (n=314; PY=687.6)
Any AE	240.2 (228.0, 252.9)	268.0 (256.0, 280.4)	292.5 (279.8, 305.5)
Any serious AE	10.8 (8.3, 13.8)	12.2 (9.8, 15.1)	16.3 (13.4, 19.6)
Any AE leading to discontinuation of study drug	6.5 (4.6, 8.9)	7.3 (5.4, 9.5)	7.7 (5.8, 10.1)
Any death ^a	0.7 (0.2, 1.7)	0.9 (0.3, 1.9)	1.0 (0.4, 2.1)
Serious infection	2.5 (1.4, 4.1)	3.3 (2.1, 4.9)	4.4 (2.9, 6.2)
Opportunistic infection excluding TB and HZ	0.2 (0.0, 0.9)	0.1 (0.0, 0.8)	0.3 (0.0, 1.1)
HZ	0.8 (0.3, 1.9)	4.5 (3.1, 6.4)	4.7 (3.2, 6.6)
Active TB	0	0.3 (0.0, 1.0)	0.3 (0.0, 1.1)
NMSC	0	0.4 (0.1, 1.2)	1.0 (0.4, 2.1)
Malignancy other than NMSC	1.0 (0.4, 2.2)	0.6 (0.2, 1.5)	1.2 (0.5, 2.3)
Hepatic disorder	14.1 (11.3, 17.5)	12.5 (10.0, 15.4)	15.0 (12.2, 18.2)
GI perforation ^b	0	0	0.4 (0.1, 1.3)
Neutropenia	2.2 (1.2, 3.7)	4.5 (3.1, 6.4)	5.7 (4.0, 7.8)
CPK elevation	1.8 (0.9, 3.3)	7.7 (5.8, 10.0)	15.4 (12.6, 18.6)
MACE ^b	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)
VTE ^b	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)

Data were censored at the time of MTX or UPA addition for rescued pts

^aIncludes treatment-emergent (≤ 30 days after the last dose of study drug) and non-treatment-emergent deaths. ^bAdjudicated

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