Figure. Proportion of pts achieving ACR20/50/70 and DAS28-4(ESR) remission at M3, stratified by sex and treatment group (P3 RCTs)

*p<0.05, **p<0.001

Pts from ORAL Standard who were found to be non-compliant with study procedures were excluded; PBO data not presented ACR20/50/70, American College of Rheumatology $\geq 20/50/70\%$ response criteria; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; n, number of responders; N, number of patients assessed at each visit

Conclusion: Efficacy outcomes with tofacitinib and ADA were generally higher in males and comparable in females vs previously reported mixed population response rates for advanced therapies. Safety findings did not reveal a consistent pattern between sexes. Tofacitinib persistence was similar between sexes.

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POS0653

IMPACT OF UPADACITINIB OR ADALIMUMAB AS INITIAL THERAPY ON THE ACHIEVEMENT OF 48-WEEK TREATMENT GOALS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE: POST HOC ANALYSIS OF A PHASE 3 STUDY

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Background: In the randomized, double-blinded, Phase 3 SELECT-COMPARE study, upadacitinib (UPA) + MTX demonstrated greater clinical and functional responses vs adalimumab (ADA) + MTX in patients (pts) with RA and inadequate responses to MTX.^{1,2} Pts with insufficient response to initial therapy were switched from UPA to ADA (and vice versa) according to treat-to-target (T2T) principles.

Objectives: We analyzed 1-year treatment outcomes in SELECT-COMPARE according to initial randomization group, regardless of whether pts subsequently switched therapy.

Methods: Pts initially randomized to UPA 15 mg once daily (QD) or ADA 40 mg every other week (EOW; both + MTX) for up to 48 weeks in SELECT-COMPARE were included in the analysis. As per the protocol-directed rescue strategy, pts

experiencing <20% improvement in tender or swollen joint counts at Week 14, 18, or 22, or Clinical Disease Activity Index (CDAI) >10 at Week 26, were switched from UPA to ADA or ADA to UPA in a blinded fashion. Efficacy outcomes included CDAI remission (≤ 2.8) and low disease activity (LDA; ≤ 10), DAS of 28 joints using CRP (DAS28(CRP)) <2.6 and ≤ 3.2 , and a composite of “deep response” (CDAI remission, HAQ-Disability Index <0.5, and pain score <20). Data are presented and attributed to initial randomized group (UPA or ADA) regardless of any subsequent switch in therapy. Time-averaged response rates were calculated as area under the curve of response rate standardized by 48 weeks. The proportions of pts who maintained Week 26 responses through 6 months of follow-up are also reported.

Results: This analysis included 651 pts initially randomized to UPA (of whom 245 switched to ADA) and 327 pts initially randomized to ADA (of whom 157 switched to UPA). Baseline characteristics including age, sex, and BMI were generally well balanced between randomized groups. At Week 48, similar proportions of pts initially randomized to UPA or ADA therapy achieved CDAI remission/LDA (27.6%/61.9% vs 24.8%/59.0%) and DAS28(CRP) <2.6/ ≤ 3.2 (45.0%/60.2% vs 43.7%/59.0%) (Figure 1). However, a small but significantly greater proportion of pts achieved a deep response with initial UPA vs initial ADA therapy (17.8% vs 12.8%; p<0.05). In addition, time-averaged response rates over 48 weeks were higher for initial UPA vs initial ADA therapy across efficacy outcomes. Similar trends were observed for other outcomes. Additionally, similar proportions of pts maintained Week 26 responses with initial UPA vs initial ADA therapy based on CDAI remission/LDA and DAS28(CRP) <2.6/ ≤ 3.2 during 6-month follow-up (Table 1).

Conclusion: Using a stringent T2T approach to RA management, rates of LDA

Figure 1. Achievement of CDAI (A) and DAS28(CRP) (B) responses corresponding with time-averaged response rates over 48 weeks by initial therapy with UPA or ADA in SELECT-COMPARE

or remission at 1 year were similar, regardless of whether pts were initially randomized to UPA or ADA. However, initial UPA therapy led to more frequent deep responses and higher time-averaged response rates vs initial ADA therapy.

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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.