

Update on new treatment options for psoriatic arthritis

OP0223

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (SELECT-PSA-2): A DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE 3 TRIAL

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Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for treatment of moderate to severe rheumatoid arthritis (RA) and currently under evaluation for treatment of psoriatic arthritis (PsA).

Objectives: To assess the efficacy and safety of UPA versus placebo (PBO) in patients (pts) with PsA and prior inadequate response or intolerance to ≥1 biologic disease-modifying anti-rheumatic drug (bDMARD).

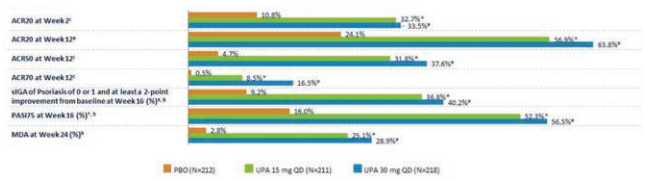
Methods: In SELECT-PSA-2, pts were randomized 1:1:1 to once daily UPA 15 mg (UPA15), UPA 30mg (UPA30), or PBO. Pts were stratified by baseline DMARD use, number of prior failed bDMARDs, and extent of psoriasis. The primary endpoint was the proportion of pts achieving ACR20 response at Wk 12. Multiplicity controlled secondary endpoints included change in HAQ-DI, FACIT-Fatigue (FACIT-F), and SF-36 Physical Component Summary (PCS) at Wk 12; static Investigator Global Assessment (sIGA) of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline, PASI75, and change in Self-Assessment of Psoriasis Symptoms (SAPS) at Wk 16; and proportion of pts achieving MDA at Wk 24. Additional key secondary endpoints were ACR50 and ACR70 at Wk 12, and ACR20 at Wk 2. Treatment-emergent adverse events (TEAEs) are reported for pts who received ≥1 dose of study drug.

Results: 641 pts were randomized and received study drug; 54.3% were female with mean age of 53.4 years, and mean duration since PsA diagnosis of 10.1 years. 61% of pts failed 1 bDMARD, 18% failed 2 bDMARDs, and 13% failed ≥3 bDMARDs. 543 (84.6%) pts completed Wk 24 study drug.

At Wk 12, a significantly greater proportion of pts receiving UPA15 and UPA30 vs PBO achieved ACR20 (56.9% and 63.8% vs 24.1%; $p < .0001$ for both comparisons). Statistically significant improvements were observed in the UPA15 and UPA30 arms vs PBO in all multiplicity controlled secondary endpoints, including ΔHAQ-DI (PBO, -0.10; UPA15, -0.30; UPA30, -0.41), ΔSF-36 PCS (PBO, 1.6; UPA15, 5.2; UPA30, 7.1), ΔFACIT-F (PBO, 1.3; UPA15, 5.0; UPA30, 6.1), and ΔSAPS (PBO, -1.5; UPA15, -24.4; UPA30, -29.7; $p < .0001$ for all endpoints; **Figure 1**). In addition, a greater proportion of pts achieved ACR50 and ACR70 at Wk 12 with UPA vs PBO. Generally, TEAEs were reported at similar frequencies in the PBO and UPA15 arms and at a higher frequency in the UPA30 arm (**Figure 2**). Numerically higher rates of serious AEs were reported in the UPA arms. Herpes zoster was more frequent with UPA30. Three malignancies occurred in each of the UPA arms. One adjudicated non-fatal myocardial infarction and one adjudicated pulmonary embolism were reported with UPA15.

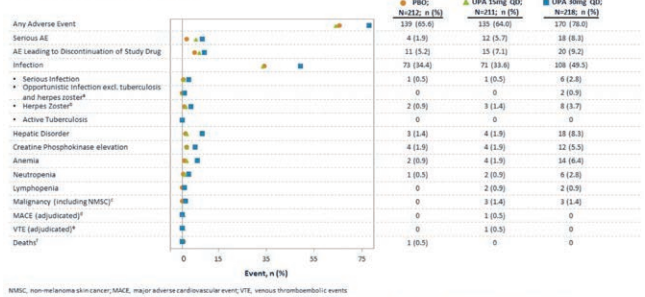
Conclusion: In this bDMARD-IR PsA population, UPA15 and UPA30 demonstrated significant improvements across PsA domains including improvements in joint and skin signs and symptoms vs PBO through Wk 24 with improvement observed by Wk 2. A greater percentage of pts treated with UPA achieved MDA and ACR50/70, stringent composite measures of disease control. No new safety signals were identified compared to what has been observed with UPA in RA.

Figure 1. Efficacy Endpoints



*Primary endpoint. †Multiplicity controlled secondary endpoints. ‡Additional secondary endpoints. *For patients with baseline sIGA 2. †For patients with ≤ 3% body surface area psoriasis at baseline. PBO, placebo; UPA, upadacitinib; QD, once daily; ACR, American College of Rheumatology; sIGA, static Investigator Global Assessment; PASI, Psoriasis Area Severity Index; MDA, Minimal Disease Activity; †, $p < .0001$ for UPA15 vs PBO, $p < .0001$ for UPA30 vs PBO. ‡Improvement from baseline provided ACR20 at Week 12 and ACR30 at Week 2. Multiplicity adjustments were applied to the primary and secondary endpoints. Results for serious endpoints are based on non-responder imputation (NRI) analysis; each of the two UPA arms was compared to PBO using the Cochran-Mantel-Haenszel (CMH) test, adjusting for the main stratification factor of corticosteroid use of at least 1 DMARD. Results for MDA at week 24 are based on NRI with additional rescue handling, where patients received at Week 18 are treated as non-responders. A graph of multiplicity testing procedure is used to control the overall type I error rate at the 0.05 level for all primary and selected secondary endpoints.

Figure 2. Safety Summary Through Week 24



NMSC, non-melanoma skin cancer; MACC, major adverse cardiovascular event; VTE, venous thromboembolic events. *Opportunistic infections: UPA30 1 case of listeria, 1 case of fungal candidiasis, herpes zoster. All events of herpes zoster were mild or moderate in severity with the exception of 1 severe event of herpes zoster involving 2 ophthalmes in 1 pt on UPA30. There are 3 cases of involvement of 2 ophthalmes (1 on UPA15 and 2 on UPA30). Malignancies: UPA15 1 pt basal cell carcinoma, 1 pt prostate cancer, 1 pt rectal cancer; UPA30 1 pt rectal adenocarcinoma, 1 pt ovarian cancer and endometrial cancer, 1 pt basal cell carcinoma. †MACC includes death, non-fatal myocardial infarction, non-fatal stroke; UPA15 1 non-fatal myocardial infarction; VTE, UPA15 1 pulmonary embolism; Death: PBO 1 motor vehicle accident.

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