Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling by key cytokines involved in psoriatic arthritis (PsA) and plaque psoriasis (PsO) pathogenesis. Deucravacitinib is a novel oral agent that selectively inhibits TYK2 via an allosteric mechanism by binding to the nonconserved regulatory domain of the kinase. A previous Phase 2 trial in PsO had demonstrated that deucravacitinib was efficacious and well tolerated, with no laboratory abnormalities observed.

Objectives: To evaluate the efficacy and safety of deucravacitinib in active PsA.

Methods: This is an ongoing, 1-year, randomized, double-blind, placebo (PBO)-controlled (initial 16 weeks), multinational, Phase 2 trial (NCT03881059). Eligible patients had a PsA diagnosis for ≥6 months, met CASPAR criteria, and had active disease with ≥3 tender and ≥3 swollen joints, C-reactive protein ≥3 mg/L (ULN, 5 mg/L), and ≥1 psoriatic lesion (≥2 cm). Patients who failed or were intolerant to ≥1 nonsteroidal anti-inflammatory drug, corticosteroid, conventional synthetic disease-modifying antirheumatic drug (csDMARD), and/or 1 TNF inhibitor (TNFi) ≥30%. Patients were randomized 1:1:1 to deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. The primary endpoint was achievement of ACR 20 response at Week 16. Additional endpoints included the proportion of patients achieving ACR 50/70 response, Health Assessment Questionnaire-Disability Index (HAQ-DI) response (≥0.35 improvement from baseline), enthesis resolution (Leeds Enthesitis Score <1), minimal disease activity, change from baseline in SF-36 physical component score (SF-36 PCS) and mental component score (SF-36 MCS), Psoriasis Area and Severity Index (PASI) 75 response, adverse events (AEs), and laboratory parameters.

Results: Of 203 patients randomized, 180 (89%) completed 16 weeks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and baseline disease characteristics were similar across groups. Mean age was 49.8 years, 51% of patients were male, median PsA duration was 4.5 years, 66% of patients used csDMARDs at baseline and throughout the study, and 15% had used a TNFi. This study met its primary endpoint, with deucravacitinib 6 mg and 12 mg QD demonstrating significantly higher ACR 20 responses versus PBO at Week 16 (Figure 1). Additional endpoints were also met with deucravacitinib versus PBO (Figure 1). Adjusted mean changes from baseline in SF-36 PCS and SF-36 MCS at Week 16, respectively, were significantly higher in the deucravacitinib 6 mg QD group (5.6 vs 2.3, P=0.0062; 3.6 vs 0.7, P=0.0211) and 12 mg QD group (5.8 vs 2.3, P=0.0042; 3.5 vs 0.7, P=0.0263) compared with PBO. PASI 75 responses were also significantly higher in the deucravacitinib groups (P=0.0136 vs PBO). The most common AEs in the deucravacitinib 6 mg/12 mg PBO groups, respectively, during the 16-week treatment period were nasopharyngitis (6.7%/17.9%/7.6%), sinusitis (0%/7.5%/0%), headache (7.1%/15.4%/4.5%), and rash (4.3%/6.0%/0%). No serious AEs, herpes zoster infections, opportunistic infections, or thrombotic events were reported in deucravacitinib-treated patients during this period. Additionally, no significant changes from baseline in hematologic parameters (lymphocytes, neutrophils, platelets, and hemoglobin) or serum lipids were observed with deucravacitinib treatment.

Conclusion: Deucravacitinib was efficacious versus PBO over 16 weeks in patients with active PsA. Treatment was generally well tolerated and the safety and laboratory parameter profile of deucravacitinib was consistent with that observed in an earlier Phase 2 PsoTrial.

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associated with mitotic nuclear division and defense response to other organ-
ism, whereas in profile 4 represented a stable-stable-increasing expression
trend and significantly associated with fatty acid metabolism and steroid metabolic process.

Conclusion: Biologics effectively reconstituted the gene signatures of psoriasis in different aspects. TSG features could be one of indicator for precise interven-
tion for psoriasis.

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