Impact of oral, selective, allosteric tyrosine kinase 2 inhibitor, deucravacitinib, on psoriasis in patients with active psoriatic arthritis: results from a phase 2 trial

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Synopsis
- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates cytokine-driven signaling, importantly regulated in psoriasis, inflammatory arthritis (psA), and psoriatic arthritis pathogenesis.
- Deucravacitinib, a selective, allosteric TYK2 inhibitor, was approved in 2021 by the US FDA, and is currently under clinical investigation for the treatment of adults with moderate-to-severe plaque psoriasis (PsO) and active psA.
- Deucravacitinib uniquely inhibits the regulatory domain of TYK2 rather than to the catalytic domain, thereby selectively and preferentially blocking the tyrosine kinase.
- Deucravacitinib has shown superior efficacy and tolerability in a variety of PsO disease characteristics across two phase 2 trials (POETYK PsO-1 and POETYK PsA-2) in patients with severe PsO.
- Deucravacitinib was efficacious on multiple measures of arthritis severity in patients with a PsA trial in active PsA.
- In patients with PsO at baseline, a greater proportion of patients achieved ≥70% reduction in Psoriasis Area and Severity Index (PASI) from baseline to Week 12 with deucravacitinib 6 mg to 12 mg once daily compared with placebo at Week 16.

Objective
- This post hoc analysis further evaluated the impact of deucravacitinib on PsO in patients with PsO in the phase 2 trial.

Methods
Phase 2 Phase 2 study design
- The 52-week, double-blind, placebo-controlled trial (NCT04986001) enrolled patients with active PsO and PsA disease as per criteria, including Response Classification for Psoriatic Arthritis (PsACR) criteria, and having active disease (≥2 tender and ≥2 swollen joints, ≥3 psoriatic joints, and ≥10% body surface area (BSA) PsO). Patients were randomized to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily.
- At Week 12, patients receiving deucravacitinib who achieved minimal disease activity status were switched to unblinded open-label deucravacitinib treatment, and those who did not achieve MDA were switched to unblinded placebo.

Phase 3 Phase 3 study design
- The 52-week, phase 3 trial (NCT04674521), enrolled patients with active PsA disease with or without PsO with baseline MDA ≥2, meeting PsACR criteria. All patients were randomized to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily.

Study endpoints
- Achievement of PsO disease activity, including new onset disease, response to PsA, and achievement of treatment to target BSA and PsO thresholds were evaluated in this analysis.
- All patients were seen weekly.

Results
- Baseline demographic and disease characteristics were generally similar across treatment groups in the phase 2 trial (Table 1).
- Table 2 illustrates the baseline PsO characteristics in the phase 2 PsA trial.
- Table 3 shows the improvements in PsO measured by PASI as measured by achievement of disease thresholds.
- Baseline characteristics were generally similar across treatment groups in the phase 3 trial.
- Table 4 demonstrates that in the phase 3 trial, deucravacitinib 6 mg QD was noninferior to apremilast 30 mg twice daily.
- Table 5 illustrates the improvements in PsO measured by PASI as measured by achievement of disease thresholds.
- Table 6 shows the improvements in PsO measured by PASI as measured by achievement of disease thresholds.
- Table 7 demonstrates the improvements in PsO measured by PASI as measured by achievement of disease thresholds.

Conclusions
- Deucravacitinib was noninferior compared with placebo in improving PsO in patients with PsO.
- Deucravacitinib was noninferior compared with placebo in improving PsO in patients with baseline BSA ≥10% and PASI >12 at Week 12.
- In patients with baseline BSA ≥10% and PASI >12 at Week 12, deucravacitinib treatment resulted in improvement in both PsO disease severity and PsA disease characteristics.

Acknowledgments
- The authors acknowledge all the study investigators, Clinical Research Organizations, and Ventyx Biosciences, and XinThera.

References