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Efficacy and Safety of Povorcitinib for Extensive Vitiligo: 52-Week Results From a Double-Blinded, Placebo-Controlled, Dose-Ranging Phase 2b Study

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Introduction & Objectives:

Vitiligo is an autoimmune disease characterized by depigmentation of skin due to the progressive loss of melanocytes. The often highly visible and chronic nature of vitiligo as well as its unpredictable disease course have negative psychosocial impacts on most patients (pts), affecting quality of life. Disease pathogenesis is largely regulated by interferon-γ activation of the Janus kinase (JAK) signaling pathway. Povorcitinib is an oral, small-molecule, selective JAK1 inhibitor with potential activity in the treatment of nonsegmental vitiligo (NSV). This phase 2b study (NCT04818346) evaluated the efficacy and safety of povorcitinib in pts with extensive NSV.

Materials & Methods:

Adults with NSV affecting ≥0.5% facial and ≥8% total body surface areas were eligible. Pts were randomized 1:1:1:1 to once daily povorcitinib 15/45/75 mg or placebo for 24 wks; subsequently, pts received povorcitinib 45 or 75 mg for an additional 28 wks, with a 24-wk off-treatment follow-up period. The primary endpoint was the percentage change from baseline in total Vitiligo Area Scoring Index (T-VASI) at Wk 24. Other endpoints included percentage of pts achieving ≥50% reduction from baseline in T-VASI (T-VASI50), ≥50%/≥75% reduction in facial VASI (F-VASI50/75), and safety.

Results:

Of 171 randomized pts, 54.4% were female and 66.7% had Fitzpatrick skin types I–III. Median (range) age was 50 (23–74) y and disease duration was 16.4 (0.8–58.9) y. At Wk 24, the primary efficacy endpoint, T-VASI percent change from baseline with povorcitinib (15 mg, –19.1%; 45 mg, –17.8%; 75 mg, –15.7%; least square means povorcitinib vs placebo, $P<0.01$) was statistically superior to placebo (+2.3%). Percentages of pts with F-VASI50 at Wk 24 were higher for povorcitinib (16.3%, 34.9%, and 23.8% for 15, 45, and 75 mg, respectively) than placebo (7.0%). Improved repigmentation was seen across treatment groups at Wk 52; mean percentage changes from baseline in T-VASI for povorcitinib 15-to-75-mg, 45-mg, 75-mg, and placebo-to-75-mg subgroups were –40.7%, –42.7%, –41.3%, and –18.1%, respectively; F-VASI mean percentage changes from baseline were –63.6%, –63.8%, –64.4%, and –54.8%, respectively. T-VASI50 was achieved by 45.2%, 37.0%, 37.9%, and 15.2%; F-VASI50 by 71.0%, 77.8%, 69.0%, and 63.6%; and F-VASI75 by 48.4%, 55.6%, 58.6%, and 45.5% of pts, respectively. A total of 34 pts entered the follow-up period, with 32 completing Wk 76. T-VASI median (range) percentage changes from Wk 52 to Wk 76 were 2.1% (–61.2%, 33.9%), 4.9% (–25.4%, 33.8%), 21.0% (3.8%, 295.1%), and –0.4% (–17.9%, 24.3%), respectively; F-VASI median (range) changes were 0% (–80.0%, 33.3%), 0% (–100.0%, 200.0%), 55.6% (–86.6%, 2900.0%), and 66.7% (–20.0%, 400.0%), suggesting durability of response after discontinuation of povorcitinib. Treatment-emergent/serious adverse events (TEAEs/SAEs) were 89.2%/2.4% among pts who received povorcitinib 45 or 75 mg through 52 wks. The most common TEAEs were COVID-19 (36.1%), blood creatine phosphokinase

increased (13.3%), acne (12.0%), fatigue (10.8%), and headache (9.6%).

Conclusion:

Oral povorcitinib was associated with substantial facial and total body repigmentation in pts with extensive NSV through 52 wks of treatment in this phase 2b study. Pts who were off treatment for 24 wks demonstrated durable response, maintaining their level of response achieved at Wk 52. All doses of povorcitinib were generally well tolerated.