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/Background: 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, 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.

Objectives: To evaluate the efficacy and safety of povorcitinib in patients with extensive nonsegmental vitiligo in a phase 2b, dose-ranging study (NCT04818346).

Methods: Adults with nonsegmental vitiligo affecting ≥0.5% facial and ≥8% total body surface areas were eligible. Patients were randomized 1:1:1:1 to once daily povorcitinib 15/45/75 mg or placebo for 24 weeks; subsequently, patients received povorcitinib 45 or 75 mg for an additional 28 weeks, with a 24-week off-treatment follow-up period. The primary endpoint was the percentage change from baseline in total Vitiligo Area Scoring Index (T-VASI) at Week 24. Other endpoints included percentage of patients 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 patients, 54.4% were female and 66.7% had Fitzpatrick skin types I–III. Median (range) age was 50 (23–74) years and disease duration was 16.4 (0.8–58.9) years. At Week 24, the primary efficacy endpoint, T-VASI percentage 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 patients achieving F-VASI50 at Week 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 Week 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 patients, respectively. A total of 34 patients entered the follow-up period, with 32 completing Week 76. T-VASI mean percentage changes from baseline to Week 76 were –41.3%, –43.6%, –27.1%, and –34.8%, respectively; F-VASI mean changes were –48.9%, –63.0%, –46.4%, and –73.5%, suggesting durability of response after discontinuation of povorcitinib. Treatment-emergent adverse events (TEAEs) occurred in 89.2% and serious adverse events in 2.4% among patients who received povorcitinib 45 or 75 mg through 52 weeks. 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%).

Conclusions: Oral povorcitinib was associated with substantial facial and total body repigmentation in patients with extensive nonsegmental vitiligo through 52 weeks of treatment in this phase 2b study. Patients who were off treatment for 24 weeks demonstrated durable response, maintaining their level of response achieved at Week 52. All doses of povorcitinib were generally well tolerated.

Keywords: JAK1 inhibitor, oral administration, INCB054707, repigmentation, vitiligo

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NvG is a consultant and/or investigator for AbbVie, Incyte, Merck/MSD, Pfizer, and Sun Pharma; and is chair of the Vitiligo Task Force for the European Academy of Dermatology and Venereology (EADV).

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