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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Presented at: Revolutionizing Alopecic Dermatitides, Alopecia Areata, and Vitiligo (RAA) 2024
Chicago, IL, USA June 9–10, 2024

Introduction
Vitiligo is an autoimmune disease characterized by depigmentation of skin due to the progressive loss of melanocytes.
Classical pathogenesis is largely regulated by interferon-α activation of the Janus kinase (JAK) signaling pathway.
Povorcitinib (p.o., small molecule, kinase JAK1 inhibitor) was associated with substantial repigmentation in patients with extensive nonsegmental vitiligo in the 24-week randomized, placebo-controlled period of a phase 2b dose-ranging study (NCT04403334).

Objective
To evaluate the efficacy and safety of povorcitinib in patients with extensive nonsegmental vitiligo from the phase 2b, dose-ranging study following 52 weeks of treatment, as well as on safety for 24 weeks post-treatment.

Methods
Patients and Study Design
This was a randomized, placebo-controlled, dose-ranging phase 2b study evaluating the efficacy and safety of povorcitinib in adult patients with vitiligo (Figure 1).
Eligible patients were men and women aged 18–75 years, with a clinical diagnosis of nonsegmental vitiligo and disease duration of 6 months to 5 years (NCT04818346).
Assessments of vitiligo extent were made at baseline and post-treatment using the Vitiligo Area Scoring Index (VASI) and the total VASI (T-VASI) on facial Vitiligo Area Scoring Index (F-VASI) and all body VASI (100% T-VASI).
Povorcitinib was administered once daily (45 or 75 mg) for 24 weeks, with the possibility of treatment extension.
Thereafter, patients received once daily povorcitinib 45 mg (initially randomized in the 24-week treatment) for an additional 28 weeks with 52 weeks of follow-up (extension period).

Results
Patients
Of the 171 randomized patients, 54.5% were female, and 65.7% had Fitzpatrick skin type IV–VI.
The mean (SD) age was 50 (23–74) years, and mean (SD) disease duration was 19 (45.2) years.
A total of 138 (79.8%) patients received the extension period and completed 52 weeks of treatment (placebo→75 mg, 94.3%; 15→75 mg, 81.1%; 45 mg, 84.4%; 75 mg, 85.3%; n=119).
At the end of the extension period, 86.2% (n=119) of patients who received povorcitinib 45 or 75 mg through 52 weeks, as well as durability of response for 24 weeks of treatment (placebo→75 mg, 94.3%; 15→75 mg, 81.1%; 45 mg, 84.4%; 75 mg, 85.3%)

Table 1. TEAEs Among Patients Who Received Povorcitinib 45 mg or 75 mg Throughout the Placebo-Controlled Period (Week 24) and Continued to Improve Through Week 52 of Treatment

<table>
<thead>
<tr>
<th>TEAE Leading to Discontinuation</th>
<th>Placebo→75 mg</th>
<th>15 mg→75 mg</th>
<th>45 mg</th>
<th>75 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid disorders</td>
<td>6 (14.3%)</td>
<td>2 (8.3%)</td>
<td>1 (5.6%)</td>
<td>4 (8.9%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (2.5%)</td>
<td>0 (0.0%)</td>
<td>1 (5.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4.3%)</td>
<td>0 (0.0%)</td>
<td>1 (5.6%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td>Acne</td>
<td>0 (0.0%)</td>
<td>1 (4.2%)</td>
<td>0 (0.0%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>COVID-19</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Table 2. TEAEs Among Patients Who Received Povorcitinib 45 mg or 75 mg Throughout the Study (Blinitec in Vitiligo Study) Safety Population

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Placebo→75 mg</th>
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<th>45 mg</th>
<th>75 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid disorders</td>
<td>4 (9.5%)</td>
<td>1 (4.2%)</td>
<td>1 (5.6%)</td>
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<td>0 (0.0%)</td>
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</table>

Conclusions
Oral povorcitinib was associated with substantial facial and total body repigmentation in patients with extensive nonsegmental vitiligo following 52 weeks of treatment in this phase 2b study.
A large proportion of patients who received any dose of povorcitinib achieved >50% reduction from baseline in total Vitiligo Area Scoring Index (T-VASI) and F-VASI50 (48.4%–55.6%) responses at Week 52.
Durability of response was demonstrated during the 24-week post-treatment period, with maintenance of T-VASI and F-VASI scores.
Sample sizes during post-treatment follow-up were small and findings need to be confirmed in a larger population.
All doses of povorcitinib were generally well tolerated, and no serious treatment-related TEAEs were reported.

References
In the future, extensive nonsegmental vitiligo is expected to be treated with KSHV inactivation and on the use of CXCR3B blockers in vitiligo. NvG is a consultant and/or investigator for AbbVie, ACM Pharma, Almirall, Amgen, Astellas, Bristol Myers Squibb, Calypso, Celgene, Galderma, GlaxoSmithKline, Incyte, Janssen, Merck/MSD, Novartis, Overtone Therapeutics, Pfizer, Rani, Rapt, Roche, Sanofi, Schering-Plough, Shionogi, and Ventyx and received grants and/or honoraria from AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. TP has received grants from Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, GSK, Johnson & Johnson, Merck/MSD, Novartis, Sanofi, and Ventyx; acted as a clinical study investigator (institution has received clinical study funds) for Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, GSK, Janssen, Merck/MSD, and Sanofi; and is chair of the Vitiligo Task Force for the European Academy of Dermatology and Venereology. KE is a consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. TP has received grants from Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, GSK, Johnson & Johnson, Merck/MSD, Novartis, Sanofi, and Ventyx; acted as a clinical study investigator (institution has received clinical study funds) for Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, GSK, Janssen, Merck/MSD, and Sanofi; and is chair of the Vitiligo Task Force for the European Academy of Dermatology and Venereology.