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Application of Exposure-Response Modeling to Inform the Phase 3 Dose Selection of Povorcitinib in Nonsegmental Vitiligo

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Objective

- To describe exposure-response modeling of efficacy, safety, and biomarkers to predict response rates for doses not evaluated in phase 2 and inform povorcitinib dose selection for phase 3 studies (STOP-V1/STOP-V2)

Conclusions

- **Based on exposure-response modeling, povorcitinib 30 mg QD was predicted to have more favorable efficacy and biomarker profiles vs 15 mg QD, and to have similar efficacy and biomarker profiles with a more favorable safety profile vs 45 and 75 mg QD**
- **Thus, povorcitinib 30 mg QD, a dose not tested in phase 2, was predicted to optimize the risk–benefit profile and was selected for use in phase 3 vitiligo studies (STOP-V1/STOP-V2 [NCT06113445/NCT06113471])**

Abbreviations

C_{ave}, steady-state average concentration; C_{ave} ADAY7, C_{ave} based on average dose in 7 days before visit; CXCL10/12, C-X-C motif chemokine ligand 10/12; F-VASI, facial Vitiligo Area Scoring Index; F-VASI50/75, ≥50%/≥75% improvement in F-VASI; IFN-γ, interferon-gamma; JAK, Janus kinase; NSV, nonsegmental vitiligo; OSM, oncostatin M; PK, pharmacokinetic; Q, quartile; QD, once daily; STAT, signal transducer and activator of transcription; TEAE, treatment-emergent adverse event; T-VASI, total Vitiligo Area Scoring Index; T-VASI50, ≥50% improvement in T-VASI.

Disclosures

JW, XG, KB, KH, KS, and VSP are employees and shareholders of Incyte Corporation. DPG is an employee of Parexel International, a paid consultant of Incyte Corporation. KE is a consultant for AbbVie, Incyte Corporation, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. AGP has served as an investigator for Avita, Clinuvel, and Incyte Corporation; has served as a consultant for AbbVie, Avita, Boehringer Ingelheim, Incyte Corporation, Lilly, Pfizer, Sun Pharma, Thalocan, Villaris, Vimela, Vyne, and WCG; and is a shareholder of Tara Medical.

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References

1. McElroy J, et al. *J Dermatol Physician Assist*. 2025;19(1):28-35. **2.** Zhuo J, et al. *J Med Chem*. 2026;doi:10.1021/acs.jmedchem.5c03753:[Epub ahead of print]. **3.** Pandya AG, et al. *J Am Acad Dermatol*. 2025;93(4):946-955. **4.** Wang XX, et al. *Br J Dermatol*. 2016;174(6):1318-1326.

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Introduction

- Vitiligo pathophysiology is largely driven through the JAK-STAT signaling pathway, which is activated by IFN-γ and leads to production of chemokines and recruitment of cytotoxic T cells[1]
- Povorcitinib is an oral highly selective JAK1 inhibitor[2] that is being evaluated for the treatment of several autoimmune and inflammatory diseases, including vitiligo
- In a phase 2, randomized, dose-ranging study in adults with extensive NSV (NCT04818346), povorcitinib demonstrated substantial repigmentation and was well tolerated at 15 mg, 45 mg, and 75 mg QD to Week 24 (placebo-controlled) and 45 mg and 75 mg QD to Week 52 (double-blind extension)[3]
  - No clear dose-response was observed between povorcitinib doses

Methods

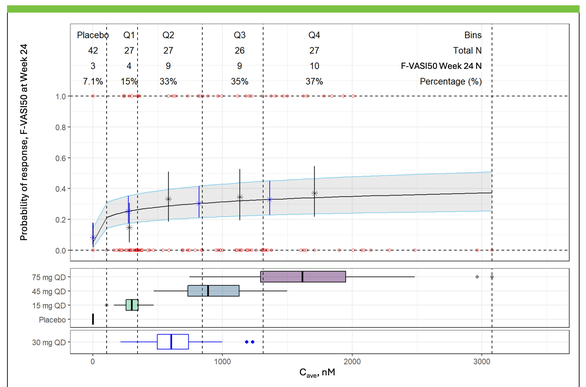
- The relationships between povorcitinib exposures (C_{ave} or C_{ave} ADAY7) and probability of efficacy, safety, and biomarker outcomes based on observed phase 2 dose-ranging data were quantified using logistic regression models
  - In the phase 2 study, a total of 171 patients were randomized to povorcitinib (15 mg QD [n=43]; 45 mg QD [n=43]; 75 mg QD [n=42]) or placebo QD (n=43)
    - At Week 24, patients initially randomized to povorcitinib 15 mg or placebo QD switched to povorcitinib 75 mg QD until Week 52; patients initially randomized to povorcitinib 45 or 75 mg QD maintained treatment[3]
- Modeled outcomes included the probability of F-VASI50 at Week 24, F-VASI75 at Week 52, and T-VASI50 at Week 52 (exposure-efficacy modeling); the probability of acne and fatigue, which were among the most common TEAEs with povorcitinib during the phase 2 study,[3] through Week 24 (exposure-safety modeling); and the probability of ≥50% decrease in CXCL10, a validated biomarker of vitiligo,[4] at Week 24 (exposure-biomarker modeling)
- A population PK model describing the time-course of concentrations following povorcitinib dosing was used to predict exposures for 30 mg QD, which served as input for efficacy and safety outcome predictions

Results

Exposure-Efficacy Modeling

- Of the dichotomous endpoints assessed in the phase 2 study, F-VASI50 had the highest number of responders at Week 24 (16.3%, 34.9%, and 23.8% in the povorcitinib 15-, 45-, and 75-mg QD groups, respectively)[3] and therefore had the most available data at this time point for use in the model
  - Achievement of F-VASI50 at Week 24 correlated with achievement of F-VASI75 at Week 52, the primary endpoint for phase 3 studies
- Predicted F-VASI50 response rates at Week 24 plateaued at exposures approximating 30 mg QD (**Figure 1**)

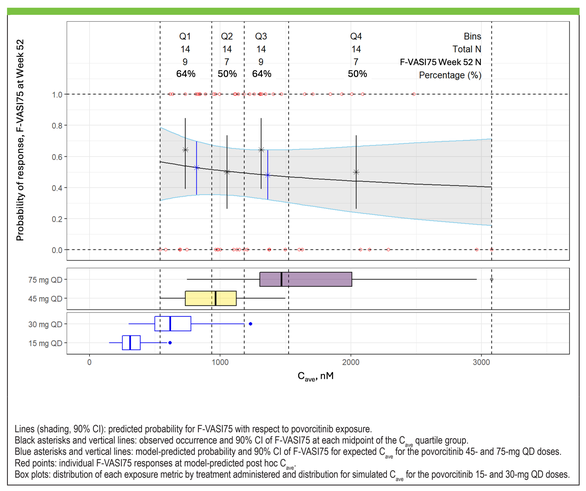
Figure 1. Observed and Predicted F-VASI50 vs Povorcitinib Exposure at Week 24



Line (shading, 90% CI): predicted probability for F-VASI50 with respect to povorcitinib exposure.
Black asterisks and vertical lines: observed occurrence and 90% CI of F-VASI50 at each midpoint of the C_{ave} quartile group.
Blue asterisks and vertical lines: model-predicted probability and 90% CI of F-VASI50 for expected C_{ave} for the placebo and povorcitinib 15-, 45-, and 75-mg QD doses.
Red points: individual F-VASI50 responses at model-predicted post hoc C_{ave}.
Box plots: distribution of each exposure metric by treatment administered during the placebo-controlled period and distribution for simulated C_{ave} for a povorcitinib 30-mg QD dose.

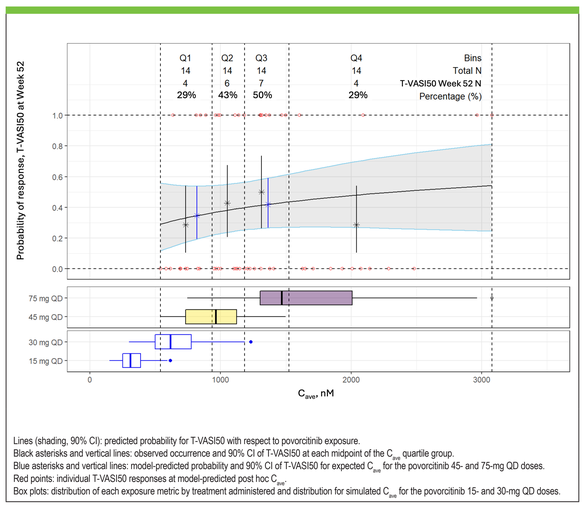
- Predicted F-VASI75 and T-VASI50 response rates at Week 52 suggested no efficacy benefit at doses beyond 45 mg QD (**Figure 2** and **Figure 3**)

Figure 2. Observed and Predicted F-VASI75 vs Povorcitinib Exposure at Week 52



Lines (shading, 90% CI): predicted probability for F-VASI75 with respect to povorcitinib exposure.
Black asterisks and vertical lines: observed occurrence and 90% CI of F-VASI75 at each midpoint of the C_{ave} quartile group.
Blue asterisks and vertical lines: model-predicted probability and 90% CI of F-VASI75 for expected C_{ave} for the povorcitinib 45- and 75-mg QD doses.
Red points: individual F-VASI75 responses at model-predicted post hoc C_{ave}.
Box plots: distribution of each exposure metric by treatment administered and distribution for simulated C_{ave} for the povorcitinib 15- and 30-mg QD doses.

Figure 3. Observed and Predicted T-VASI50 vs Povorcitinib Exposure at Week 52

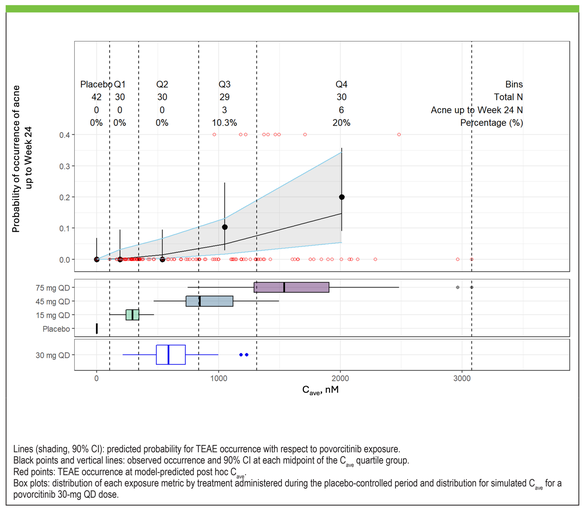


Lines (shading, 90% CI): predicted probability for T-VASI50 with respect to povorcitinib exposure.
Black asterisks and vertical lines: observed occurrence and 90% CI of T-VASI50 at each midpoint of the C_{ave} quartile group.
Blue asterisks and vertical lines: model-predicted probability and 90% CI of T-VASI50 for expected C_{ave} for the povorcitinib 45- and 75-mg QD doses.
Red points: individual T-VASI50 responses at model-predicted post hoc C_{ave}.
Box plots: distribution of each exposure metric by treatment administered and distribution for simulated C_{ave} for the povorcitinib 15- and 30-mg QD doses.

Exposure-Safety Modeling

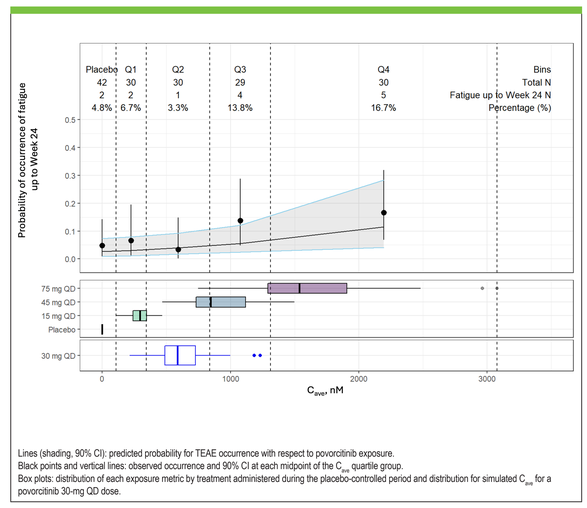
- All tested doses of povorcitinib were generally well tolerated in the phase 2 study, with no dose-related trends for grade ≥3 TEAEs[3]
- Increasing probability of acne (**Figure 4**) and fatigue (**Figure 5**) was predicted at exposures related to doses >30 mg QD, which is consistent with dose-dependent increases in frequency of these TEAEs in the phase 2 study (0%, 7.3%, and 14.3% for acne and 7.0%, 7.3%, and 14.3% for fatigue at Week 24 among patients who received povorcitinib 15, 45, and 75 mg QD, respectively, in the placebo-controlled period)[3]

Figure 4. Observed and Predicted Occurrence of Acne vs Povorcitinib Exposure Through Week 24



Lines (shading, 90% CI): predicted probability for TEAE occurrence with respect to povorcitinib exposure.
Black points and vertical lines: observed occurrence and 90% CI at each midpoint of the C_{ave} quartile group.
Red points: TEAE occurrence at model-predicted post hoc C_{ave}.
Box plots: distribution of each exposure metric by treatment administered during the placebo-controlled period and distribution for simulated C_{ave} for a povorcitinib 30-mg QD dose.

Figure 5. Observed and Predicted Occurrence of Fatigue vs Povorcitinib Exposure Through Week 24

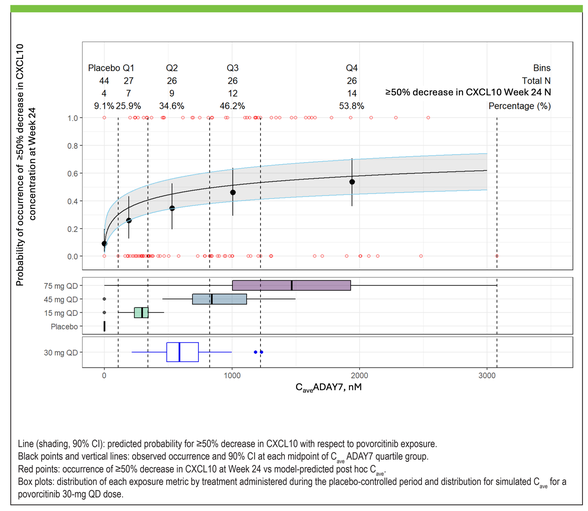


Lines (shading, 90% CI): predicted probability for TEAE occurrence with respect to povorcitinib exposure.
Black points and vertical lines: observed occurrence and 90% CI at each midpoint of the C_{ave} quartile group.
Box plots: distribution of each exposure metric by treatment administered during the placebo-controlled period and distribution for simulated C_{ave} for a povorcitinib 30-mg QD dose.

Exposure-Biomarker Modeling

- All tested phase 2 doses of povorcitinib had biological activity based on changes in biomarkers
  - However, 15 mg QD was comparable to placebo for certain biomarkers of potential relevance to vitiligo, including OSM and CXCL12
- The probability of achieving ≥50% decrease in CXCL10 at Week 24 increased with higher doses, with minimal additional gain predicted at exposures related to doses >30 mg QD (**Figure 6**)

Figure 6. Observed and Predicted Achievement of ≥50% Decrease in CXCL10 vs Povorcitinib Exposure at Week 24



Line (shading, 90% CI): predicted probability for ≥50% decrease in CXCL10 with respect to povorcitinib exposure.
Black points and vertical lines: observed occurrence and 90% CI at each midpoint of C_{ave} ADAY7 quartile group.
Red points: occurrence of ≥50% decrease in CXCL10 at Week 24 vs model-predicted post hoc C_{ave}.
Box plots: distribution of each exposure metric by treatment administered during the placebo-controlled period and distribution for simulated C_{ave} for a povorcitinib 30-mg QD dose.