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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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Presenting Author Disclosures

- Consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio

Introduction

- Vitiligo is an autoimmune disease characterized by depigmentation of skin due to the progressive loss of melanocytes[1]
- Disease pathogenesis is largely regulated by IFN-γ activation of the JAK signaling pathway[2]
- Povorcitinib (an oral, small-molecule, selective 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 (NCT04818346)[3]
- **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 durability of response for 24 weeks post-treatment

IFN-γ, interferon gamma; JAK, Janus kinase.

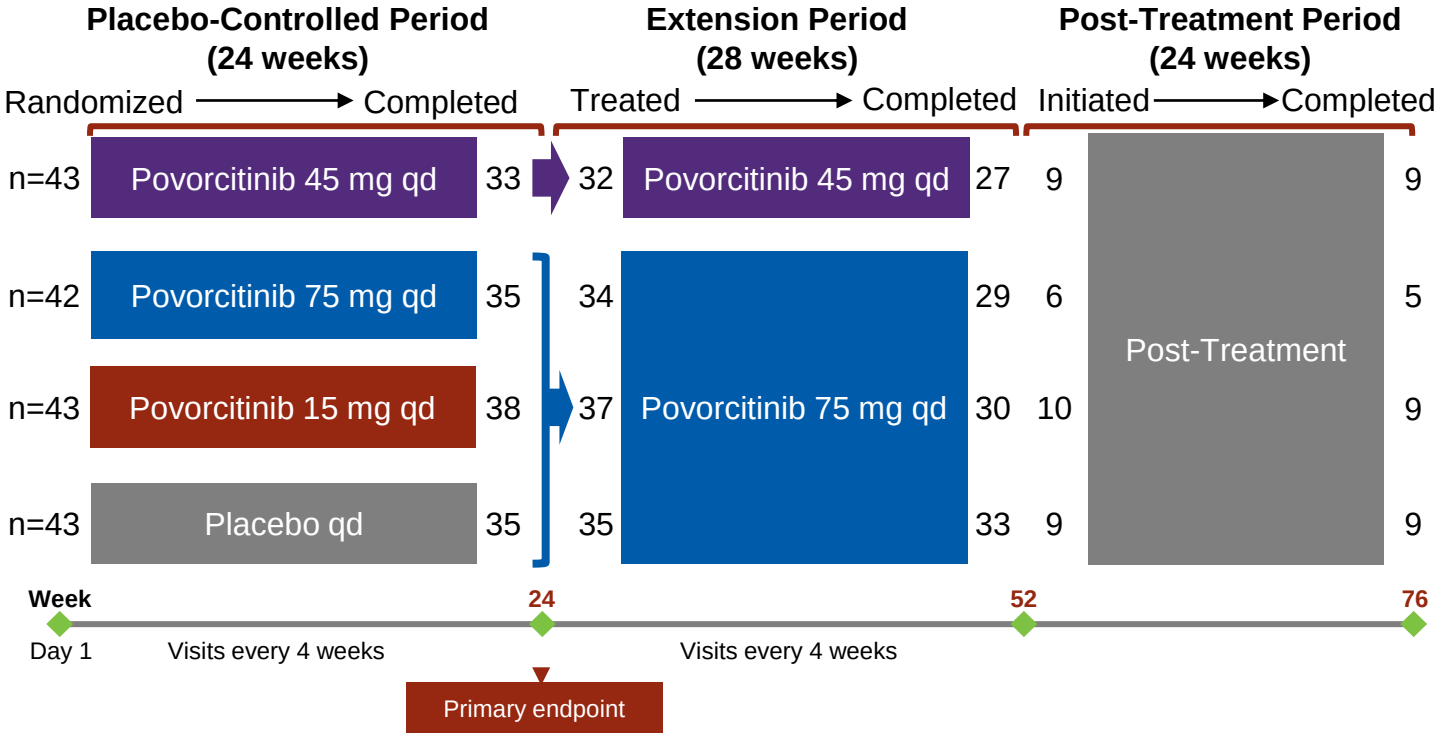
1. Rodrigues M, et al. *J Am Acad Dermatol*. 2017;77(1):1-13. **2.** Rashighi M, Harris JE. *Ann Transl Med*. 2015;3(21):343. **3.** Pandya A, et al. Presented at: American Academy of Dermatology (AAD) Annual Meeting; March 17–21, 2023; New Orleans, LA.

Study Design (NCT04818346)

Patient population:
- Adults 18–75 years old
- Nonsegmental vitiligo
- Vitiligo-affected BSA*:
  - Total body ≥8%
  - Face ≥0.5%
- VASI score:
  - T-VASI ≥8
  - F-VASI ≥0.5

Efficacy assessments:
- % change from baseline in T-VASI† and F-VASI
- % patients achieving T-VASI50, F-VASI50, and F-VASI75

Safety assessments:
Incidence of TEAEs



* Total and facial BSA were locally assessed. † Week 24 assessment was the primary endpoint.
BSA, body surface area; F-VASI, facial VASI; F-VASI50/75, ≥50%/≥75% reduction from baseline in F-VASI; qd, once daily; TEAE, treatment-emergent adverse event; T-VASI, total VASI; T-VASI50, ≥50% reduction from baseline in T-VASI; VASI, Vitiligo Area Scoring Index.

Baseline Demographics and Clinical Characteristics

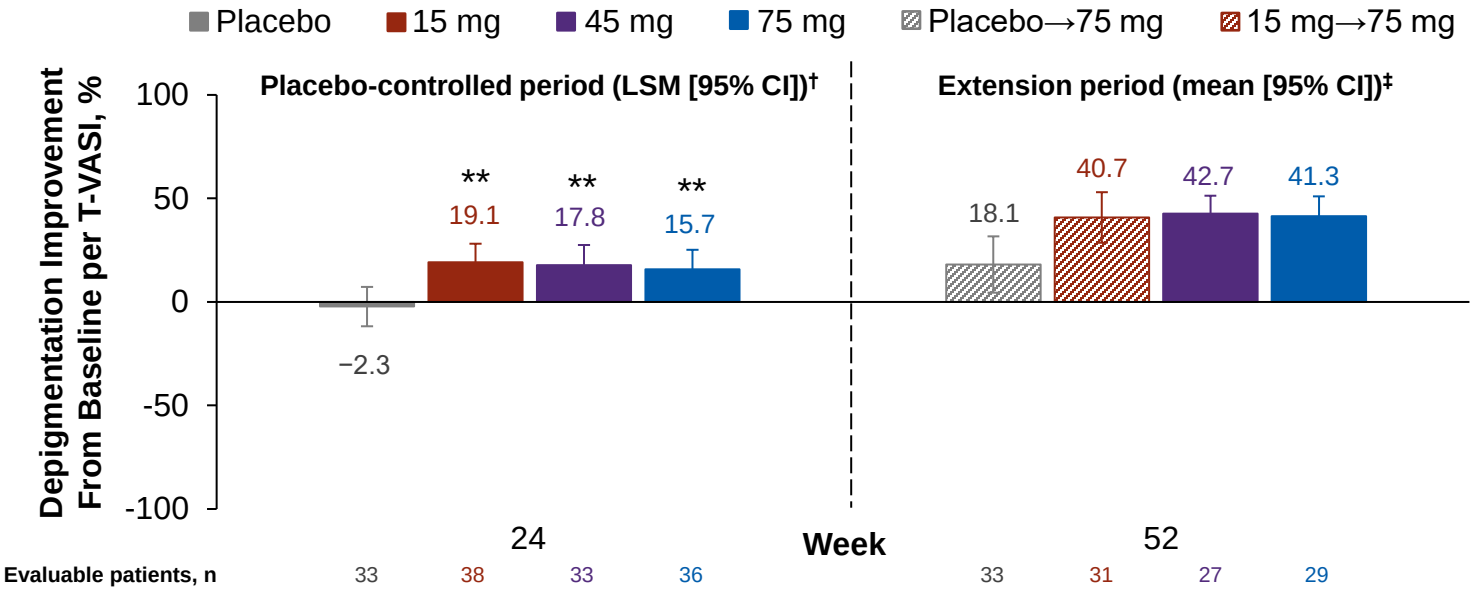
Characteristic	Placebo (n=43)	Povorcitinib 15 mg (n=43)	Povorcitinib 45 mg (n=43)	Povorcitinib 75 mg (n=42)	Total (N=171)
Age, median (range), y	51.0 (24–72)	45.0 (23–67)	51.0 (25–72)	52.5 (24–74)	50.0 (23–74)
Female, n (%)	24 (55.8)	29 (67.4)	21 (48.8)	19 (45.2)	93 (54.4)
Race, n (%)					
White	34 (79.1)	32 (74.4)	38 (88.4)	28 (66.7)	132 (77.2)
Asian	2 (4.7)	4 (9.3)	0	7 (16.7)	13 (7.6)
Black	2 (4.7)	3 (7.0)	1 (2.3)	3 (7.1)	9 (5.3)
Hispanic, n (%)	8 (18.6)	6 (14.0)	11 (25.6)	7 (16.7)	32 (18.7)
Fitzpatrick skin type, n (%)					
I–III	28 (65.1)	26 (60.5)	35 (81.4)	25 (59.5)	114 (66.7)
IV–VI	15 (34.9)	17 (39.5)	8 (18.6)	17 (40.5)	57 (33.3)

Characteristic	Placebo (n=43)	Povorcitinib 15 mg (n=43)	Povorcitinib 45 mg (n=43)	Povorcitinib 75 mg (n=42)	Total (N=171)
Baseline F-VASI, mean (SD)	1.5 (0.8)	1.3 (0.8)	1.3 (0.8)	1.1 (0.7)	1.3 (0.8)
Baseline T-VASI, mean (SD)	28.3 (21.5)	27.1 (20.1)	23.6 (19.8)	22.7 (14.2)	25.5 (19.1)
Duration of disease, mean (SD), y	19.5 (14.0)	17.6 (13.0)	19.9 (15.5)	20.5 (13.7)	19.4 (14.0)
Family history of vitiligo, n (%)	15 (34.9)	9 (20.9)	11 (25.6)	14 (33.3)	49 (28.7)
Thyroid disorders, n (%)	11 (25.6)	12 (27.9)	12 (27.9)	12 (28.6)	47 (27.5)
Previous therapy,* n (%)					
Topical corticosteroid	18 (41.9)	24 (55.8)	21 (48.8)	25 (59.5)	88 (51.5)
Topical calcineurin inhibitor	14 (32.6)	13 (30.2)	17 (39.5)	20 (47.6)	64 (37.4)
Any phototherapy	20 (46.5)	17 (39.5)	13 (30.2)	27 (64.3)	77 (45.0)

* Patients could have used multiple previous lines of therapy.
F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index.

T-VASI Percentage Change From Baseline

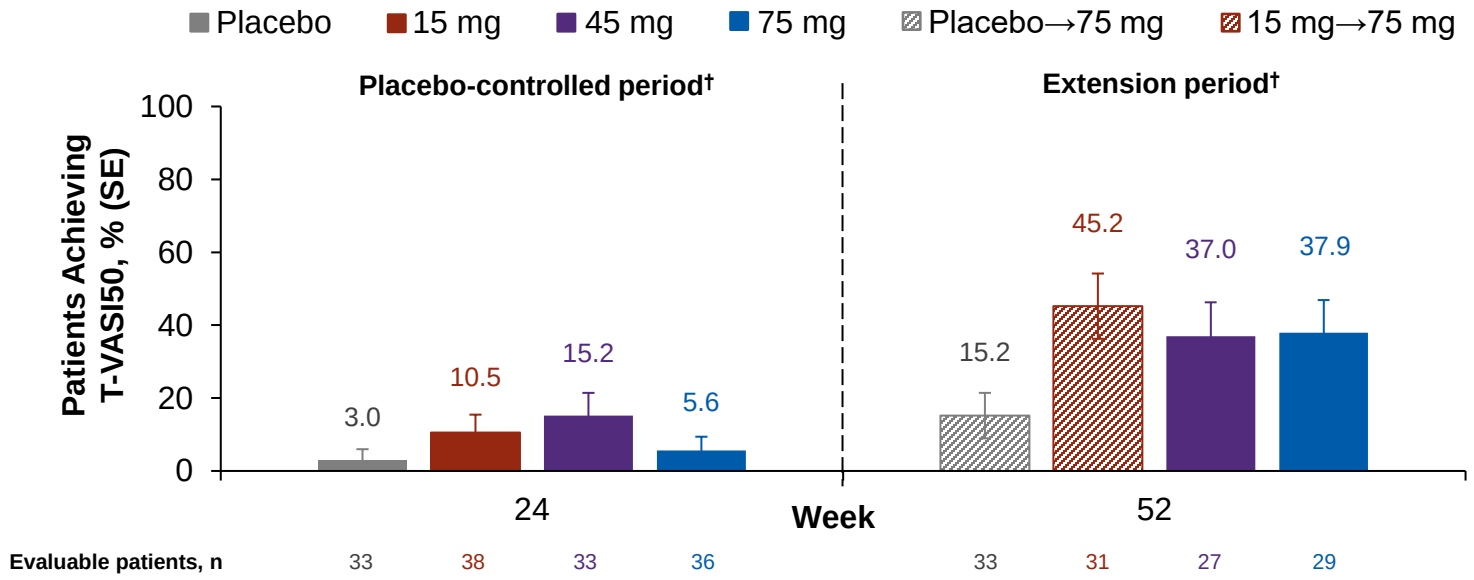
- Improvement in T-VASI was statistically superior in patients treated with povorcitinib vs placebo at Week 24 and continued to improve through Week 52 of treatment



** *P*<0.01, LSM difference vs placebo. † During the placebo-controlled period, LSM was calculated with mixed model repeated measures; data were reported as observed with no imputation. ‡ During the extension period, data were reported as observed with no imputation, and no statistical analysis was conducted.
LSM, least squares mean; T-VASI, total Vitiligo Area Scoring Index.

T-VASI50

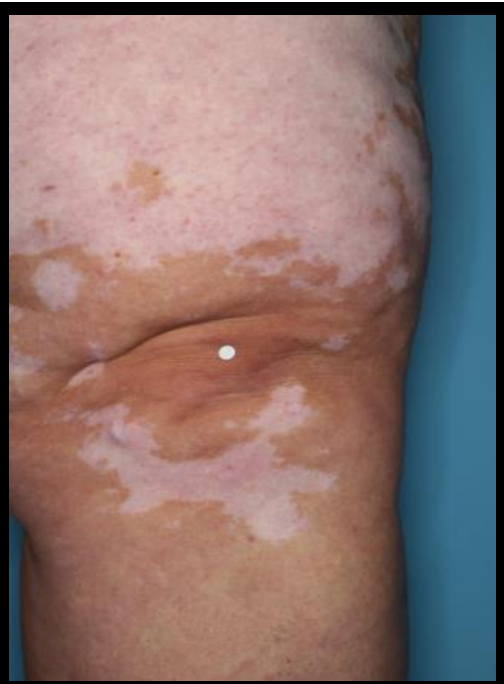
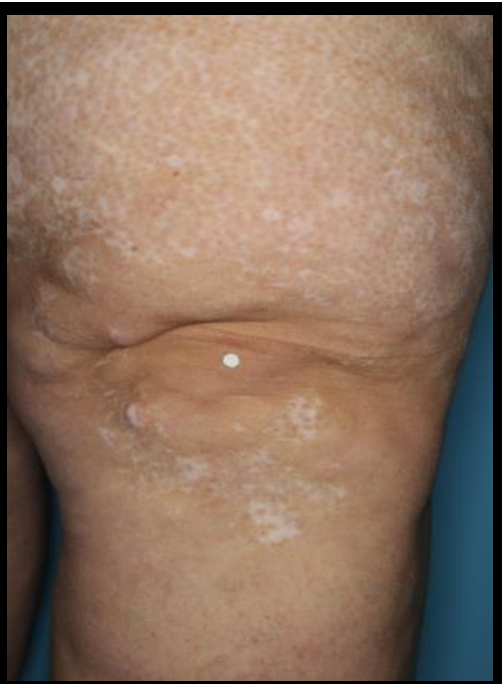
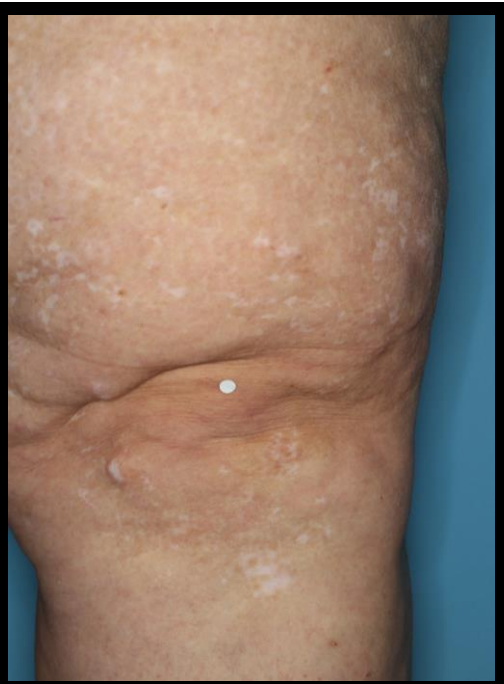
- More patients who received povorcitinib achieved T-VASI50 vs placebo at Week 24 and continued to improve through Week 52 of treatment



† Data were reported as observed with no imputation, and no statistical analysis was conducted.
T-VASI50, ≥50% reduction from baseline in total Vitiligo Area Scoring Index.

Clinical Images Showing T-VASI Response

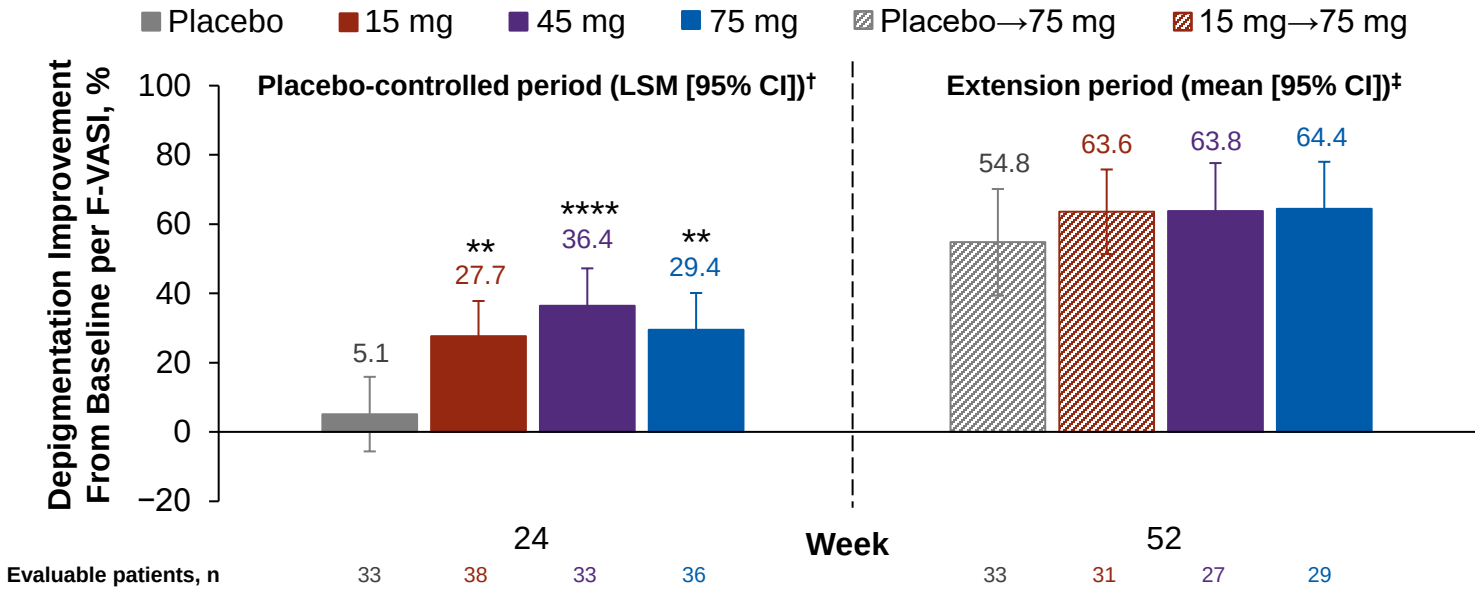
Povorcitinib 15 mg to 75 mg

Baseline	Week 24	Week 52
		
T-VASI: 61.5	**T-VASI: 41.9**	**T-VASI: 21.0**
T-VASI percentage improvement from baseline:	**31.8%**	**65.9%**

T-VASI, total Vitiligo Area Scoring Index.

F-VASI Percentage Change From Baseline

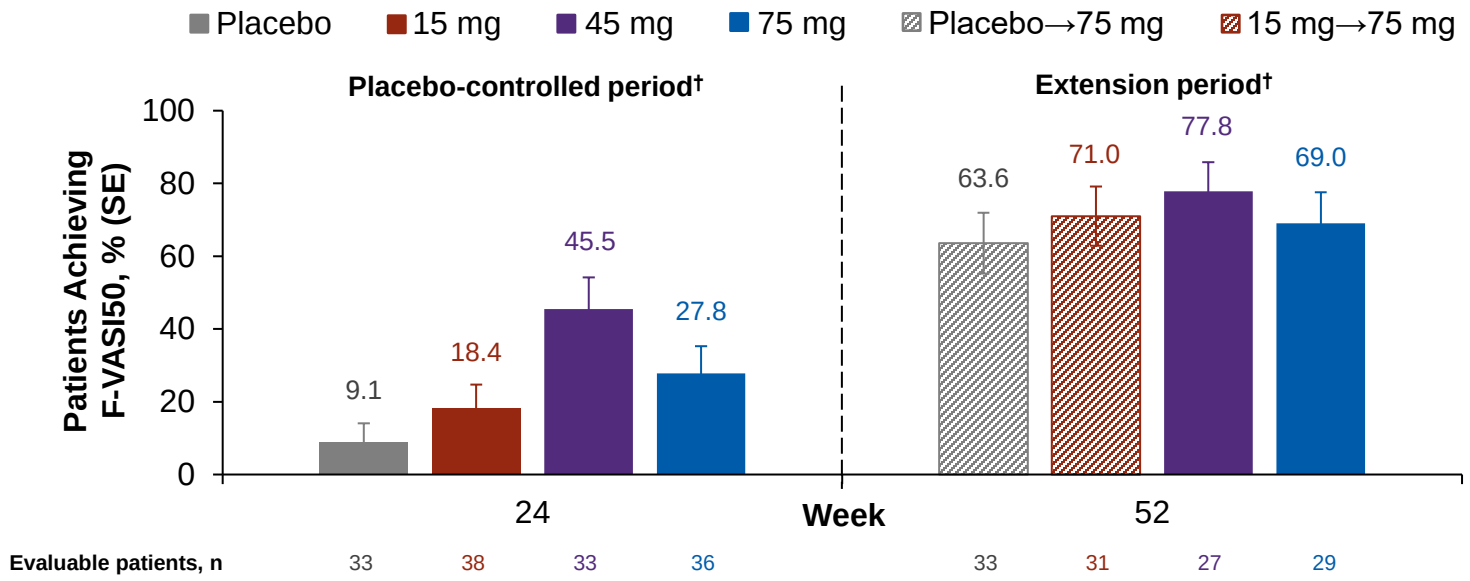
- Improvement in F-VASI was statistically superior in patients treated with povorcitinib vs placebo at Week 24 and continued to improve through Week 52 of treatment



** *P*<0.01, **** *P*<0.0001, LSM difference vs placebo. † During the placebo-controlled period, LSM was calculated with mixed model repeated measures; data were reported as observed with no imputation. ‡ During the extension period, data were reported as observed with no imputation, and no statistical analysis was conducted.
LSM, least squares mean; F-VASI, facial Vitiligo Area Scoring Index.

F-VASI50

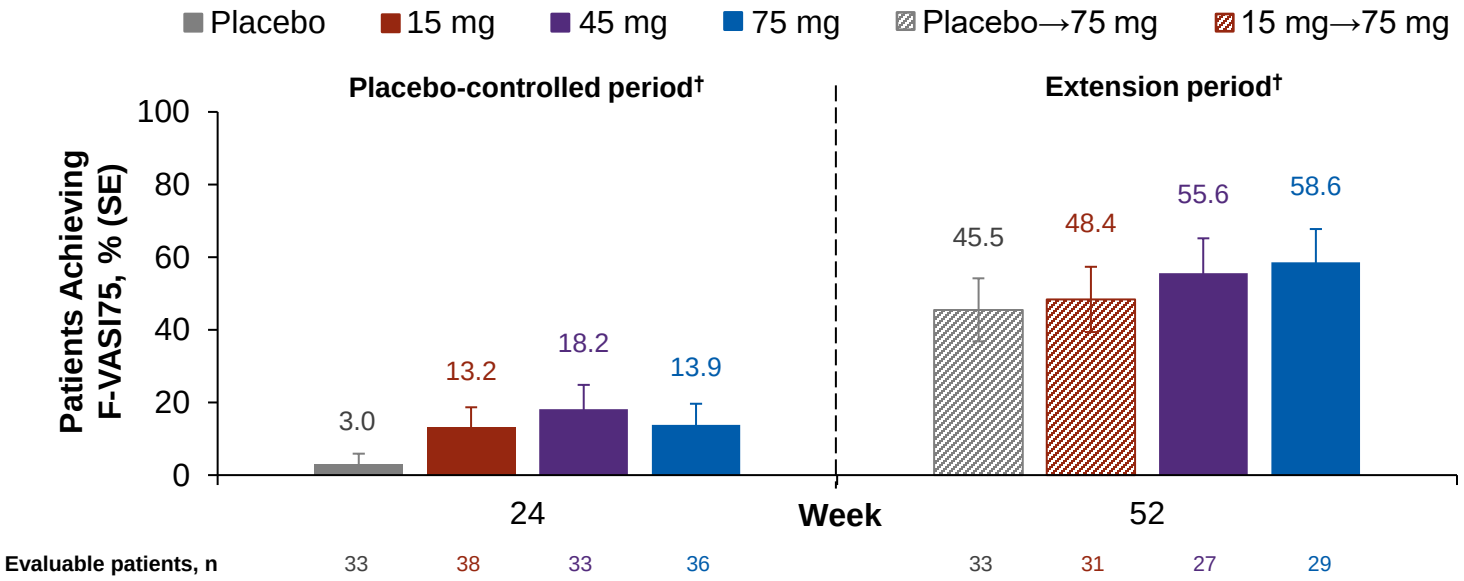
- More patients who received povorcitinib achieved F-VASI50 vs placebo at Week 24 and continued to improve through Week 52 of treatment



† Data were reported as observed with no imputation, and no statistical analysis was conducted.
F-VASI50, ≥50% reduction from baseline in facial Vitiligo Area Scoring Index.

F-VASI75

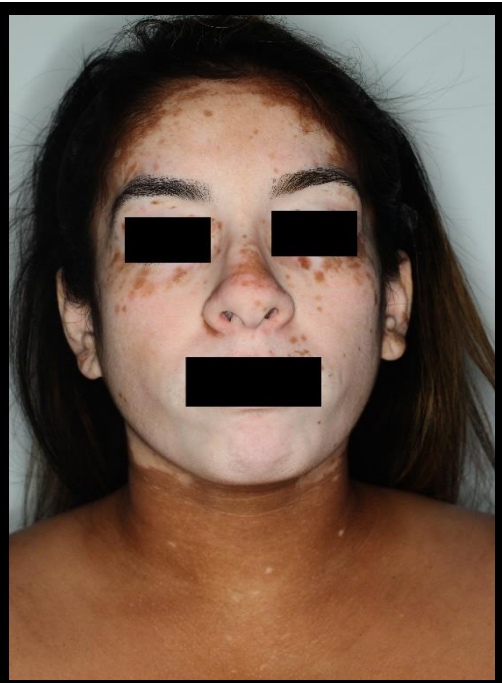
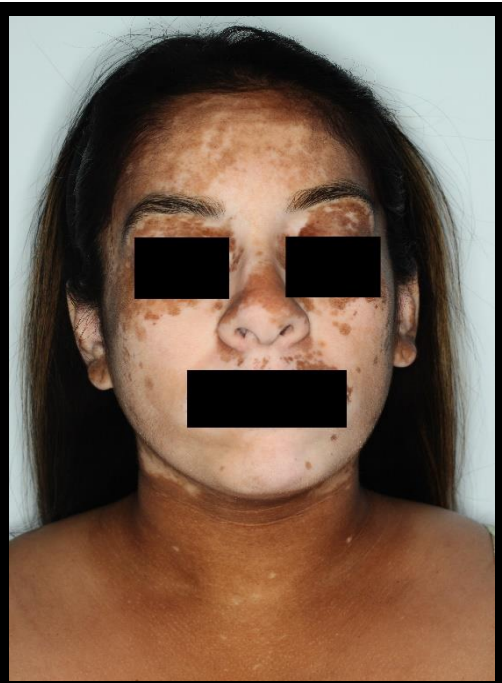
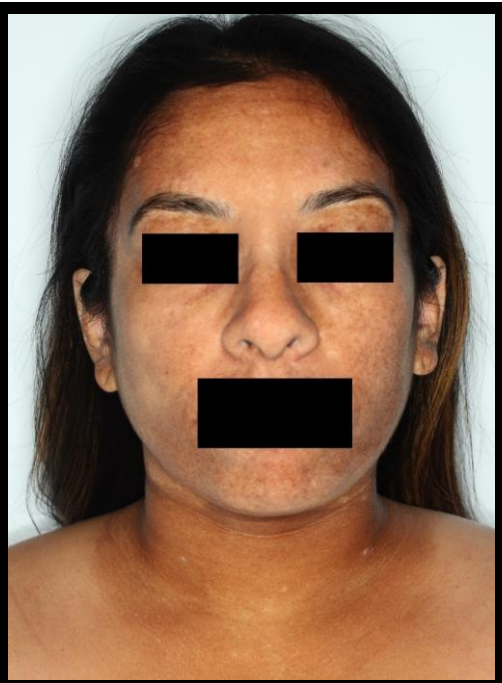
- More patients who received povorcitinib achieved F-VASI75 vs placebo at Week 24 and continued to improve through Week 52 of treatment



† Data were reported as observed with no imputation, and no statistical analysis was conducted.
F-VASI75, ≥75% reduction from baseline in facial Vitiligo Area Scoring Index.

Clinical Images Showing F-VASI Response

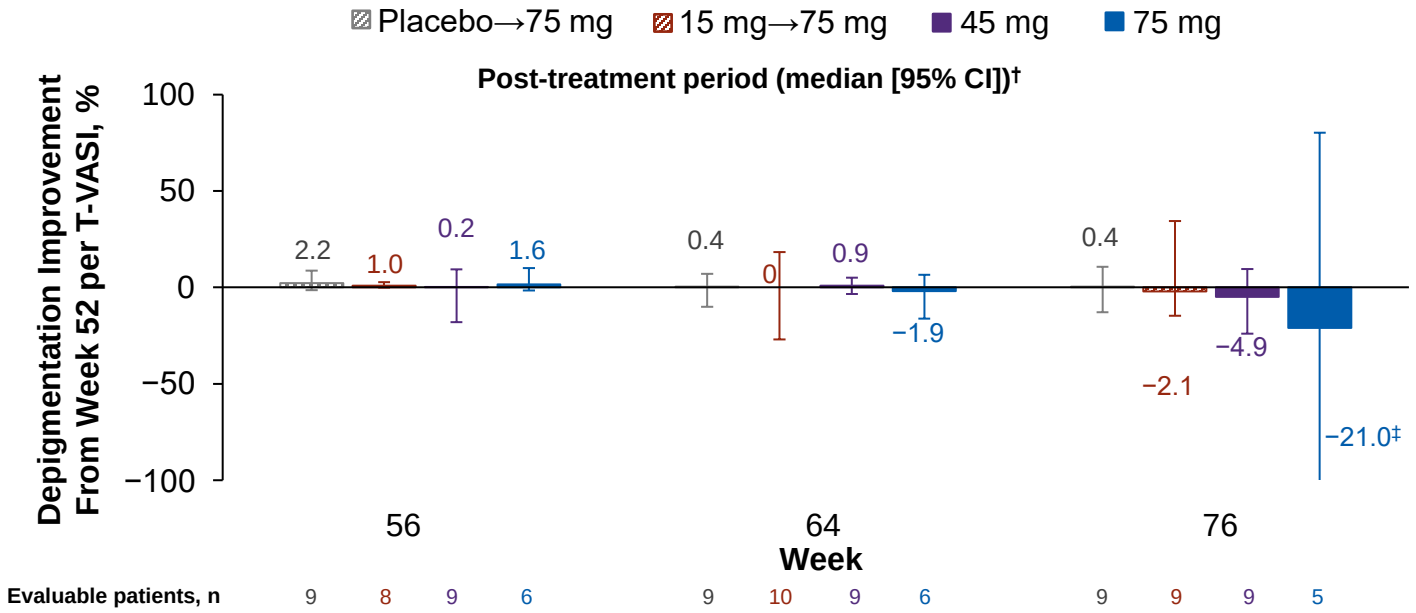
Povorcitinib 15 mg to 75 mg

Baseline	Week 24	Week 52
		
F-VASI: 2.7	**F-VASI: 1.5**	**F-VASI: 0.02**
F-VASI percentage improvement from baseline:	**44.4%**	**99.3%**

F-VASI, facial Vitiligo Area Scoring Index.

Post-Treatment T-VASI Percentage Change

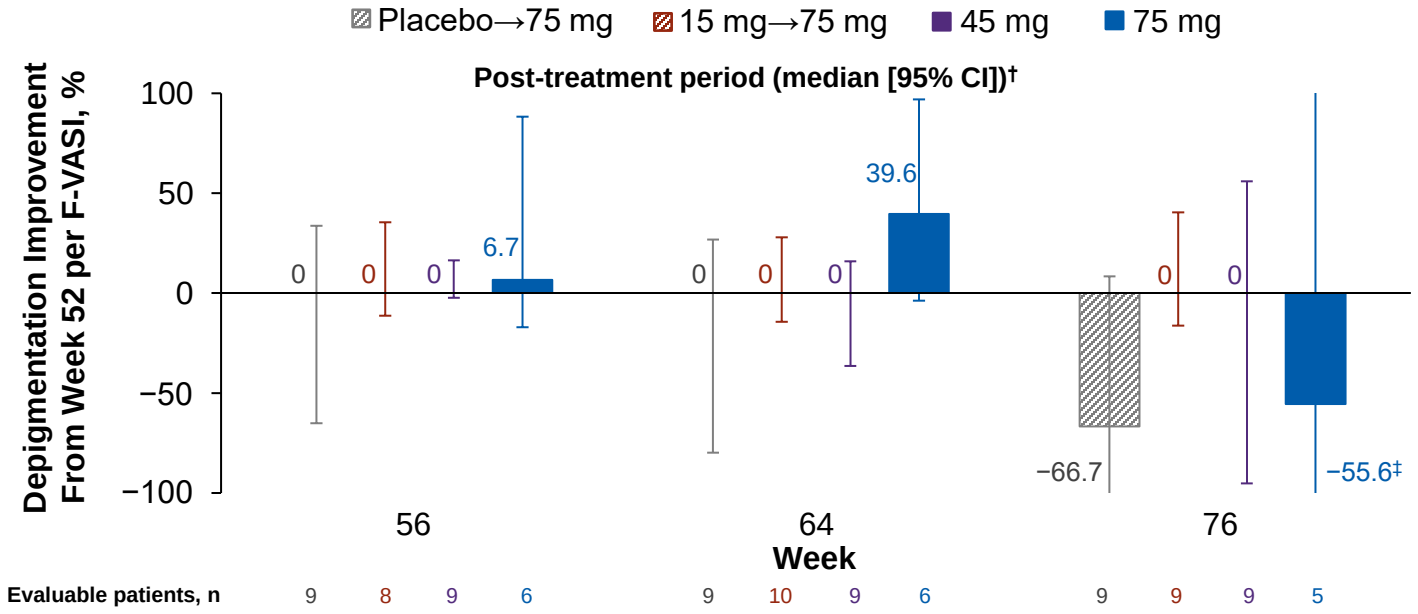
- Maintenance of T-VASI scores from Week 52 to 76 suggests off-treatment durability of response, although sample size was small, with 1 potential outlier in the 75 mg group



† During the post-treatment period, data were reported as observed with no imputation, and no statistical analysis was conducted. ‡ Improvement in T-VASI score from Week 52 to 76 with povorcitinib 75 mg was –18.0% after excluding 1 outlier; despite high Week 76 outlier values, outliers did not return to baseline VASI scores.
T-VASI, total Vitiligo Area Scoring Index.

Post-Treatment F-VASI Percentage Change

- Although sample size was small, F-VASI scores from Week 52 to 76 suggest off-treatment durability of response, with 2 potential outliers in the 75 mg group



† During the post-treatment period, data were reported as observed with no imputation, and no statistical analysis was conducted. ‡ Improvement in F-VASI score from Week 52 to 76 with povorcitinib 75 mg was 13.3% after excluding 2 outliers; despite high Week 76 outlier values, outliers did not return to baseline VASI scores.
F-VASI, facial Vitiligo Area Scoring Index.

Safety

TEAEs Throughout the Study (Baseline to Week 52)

- Among patients who received povorcitinib 45 or 75 mg through 52 weeks, TEAEs of any grade occurred in 89.2%, grade ≥3 TEAEs in 16.9%, and serious TEAEs in 2.4% of patients
- No serious TEAEs were considered related to treatment; no new safety signals were observed after Week 24

	Povorcitinib		
	45 mg (n=41)	**75 mg (n=42)**	**Total (N=83)**
Patients with TEAE, n (%)	34 (82.9)	40 (95.2)	74 (89.2)
Most common TEAEs, n (%)			
COVID-19	14 (34.1)	16 (38.1)	30 (36.1)
Blood creatinine phosphokinase increased	4 (9.8)	7 (16.7)	11 (13.3)
Acne	3 (7.3)	7 (16.7)	10 (12.0)
Fatigue	3 (7.3)	6 (14.3)	9 (10.8)
Headache	1 (2.4)	7 (16.7)	8 (9.6)
Grade 3 TEAE, n (%)	6 (14.6)	8 (19.0)	14 (16.9)
TEAE leading to discontinuation, n (%)	3 (7.3)	4 (9.5)	7 (8.4)
Serious TEAE, n (%)	1 (2.4)	1 (2.4)	2 (2.4)
Fatal TEAE, n (%)	0	0	0

TEAE, treatment-emergent adverse event.

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
- A large proportion of patients who received any dose of povorcitinib from Day 1 achieved T-VASI50 (37.0%–45.2%) and F-VASI75 (48.4%–58.6%) 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

Thank You

- We thank the study investigators, patients, and their families for their participation in this study

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