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

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Presenting Author Disclosures

- Investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte, and Pfizer
- Consultant for AbbVie, Arcutis, Avita Medical, Chromaderm, Immune Tolerance Network, Incyte, Pfizer, TWi, Viela Bio, and Villaris
- Holds stock options for Tara Medical and Zerigo Health

Background

- Vitiligo is a chronic autoimmune disease that targets melanocytes, resulting in patches of skin depigmentation[1]
- Disease pathogenesis is largely regulated by interferon-γ activation of the JAK signaling pathway[2]
- Povorcitinib is an oral, small-molecule, selective JAK1 inhibitor with potential activity in the treatment of nonsegmental vitiligo

- **Objective:** To evaluate the efficacy and safety of povorcitinib in patients with extensive nonsegmental vitiligo in a phase 2b trial (NCT04818346)

JAK, Janus kinase.

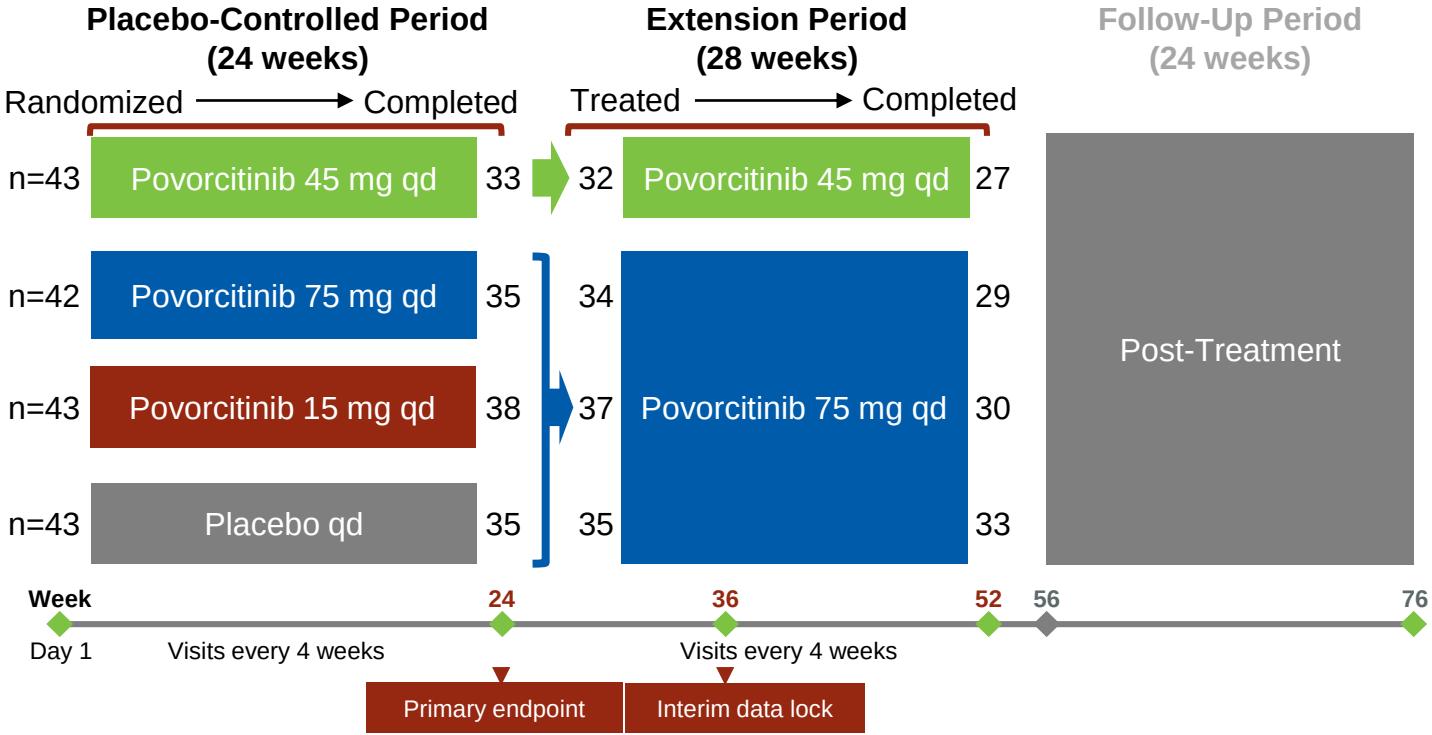
1. Rodrigues M, et al. *J Am Acad Dermatol*. 2017;77(1):1-13. **2.** Rashighi M, Harris JE. *Ann Transl Med*. 2015;3(21):343.

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†
- % patients achieving T-VASI50, F-VASI50, and F-VASI75

Safety assessments:
Incidence of TEAEs



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.
* Total and facial BSA were locally assessed. † Week 24 assessment was the primary endpoint.

Patient Demographics and Clinical Characteristics at Baseline

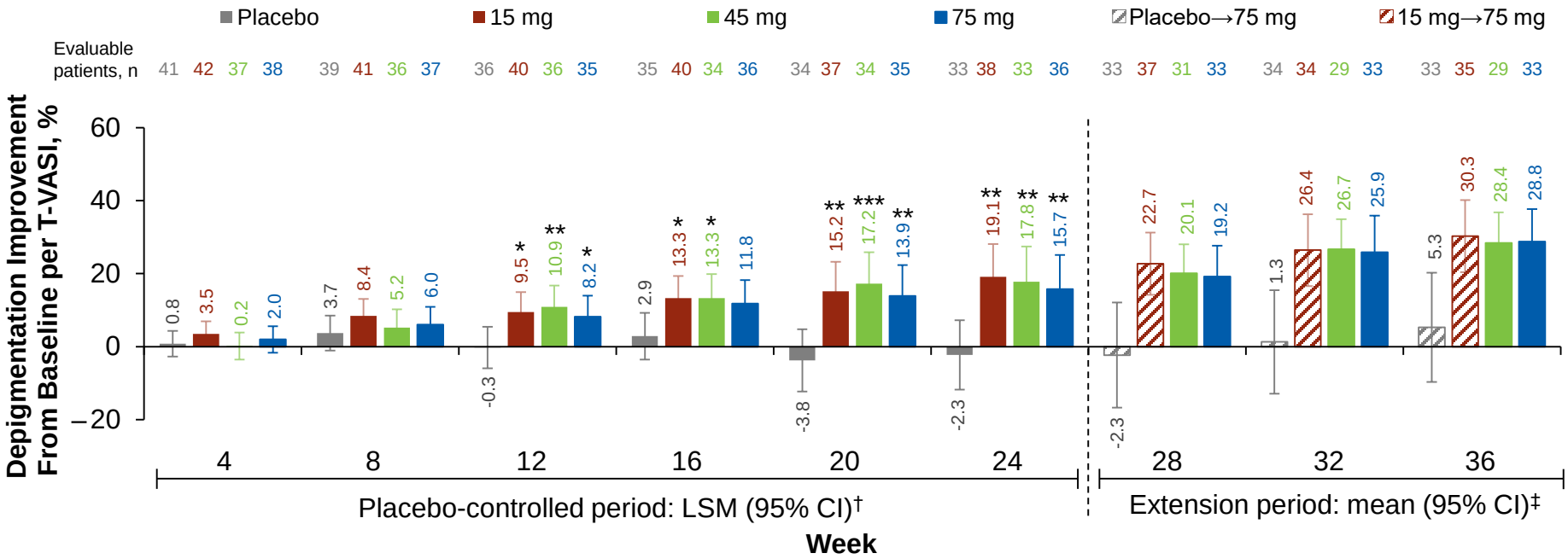
Characteristic	Placebo (n=43)	Povorcitinib 15 mg (n=43)	Povorcitinib 45 mg (n=43)	Povorcitinib 75 mg (n=42)	Total (N=171)
Age, median (range), y	51.0 (24–72)	45.0 (23–67)	51.0 (25–72)	52.5 (24–74)	50.0 (23–74)
Female, n (%)	24 (55.8)	29 (67.4)	21 (48.8)	19 (45.2)	93 (54.4)
Race, n (%)					
White	34 (79.1)	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.

T-VASI Percentage Change From Baseline

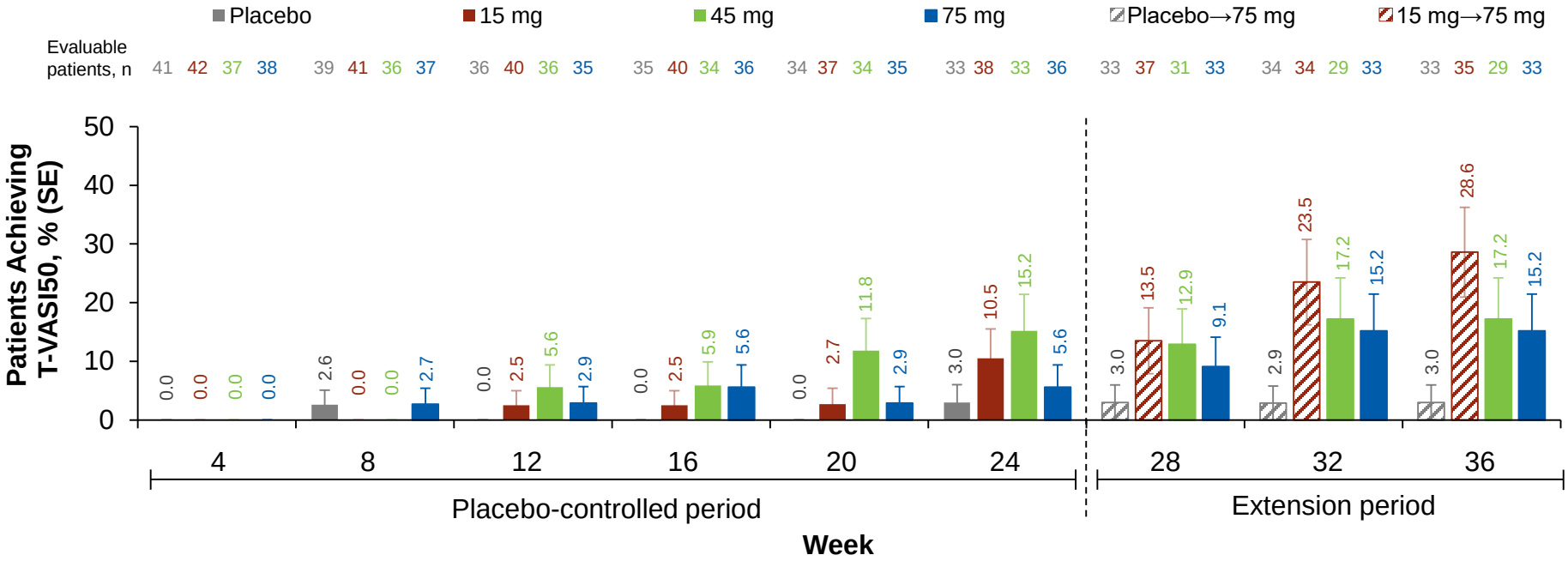
- T-VASI percentage change from baseline was statistically superior in patients treated with povorcitinib vs placebo at Week 24 and continued to improve through Week 36 of treatment



LSM, least squares mean. * *P*<0.05, LSM difference vs placebo. ** *P*<0.01, LSM difference vs placebo. *** *P*<0.001, 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.

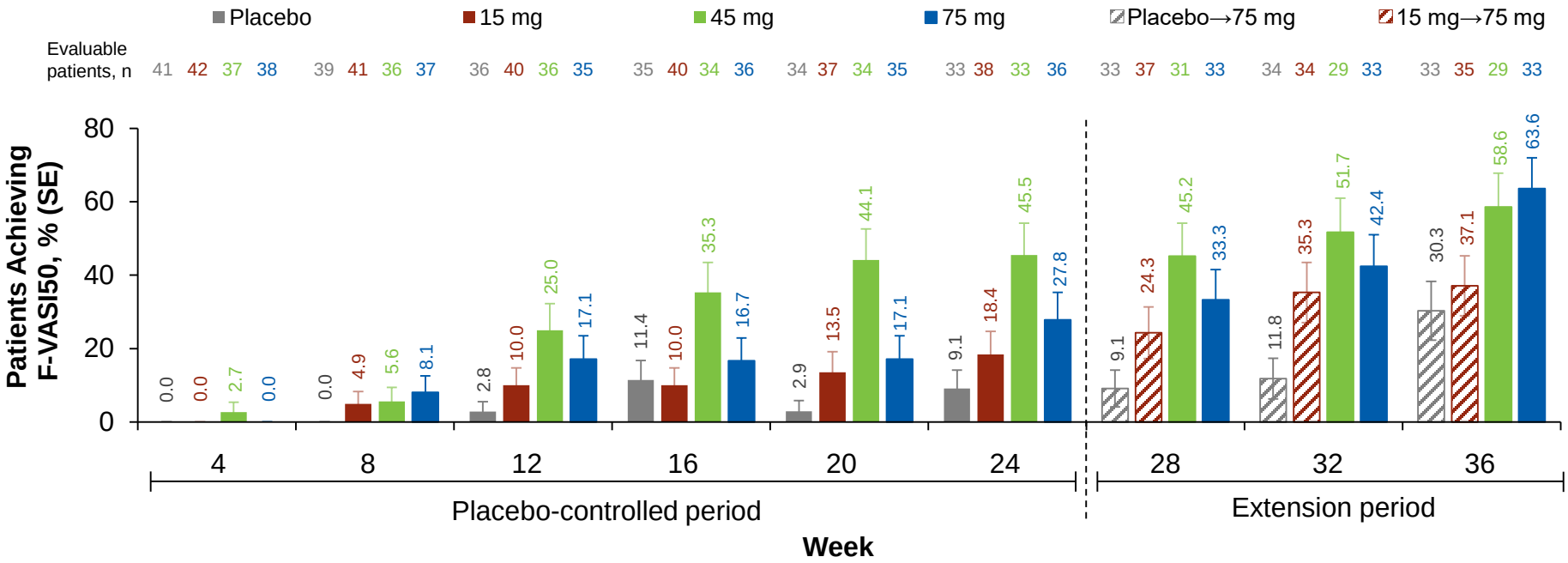
T-VASI50

- More patients who received povorcitinib achieved T-VASI50 vs placebo at Week 24 and continued to improve through Week 36 of treatment



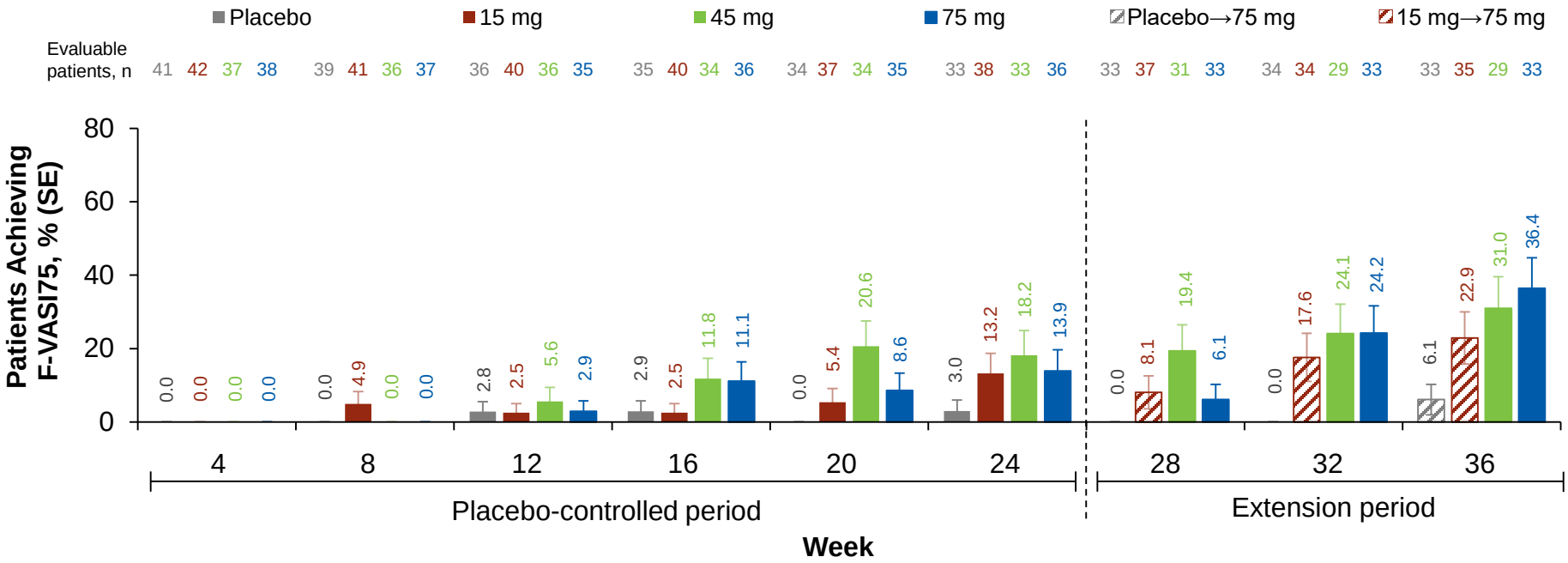
F-VASI50

- More patients who received povorcitinib achieved F-VASI50 vs placebo at Week 24 and continued to improve through Week 36 of treatment



F-VASI75

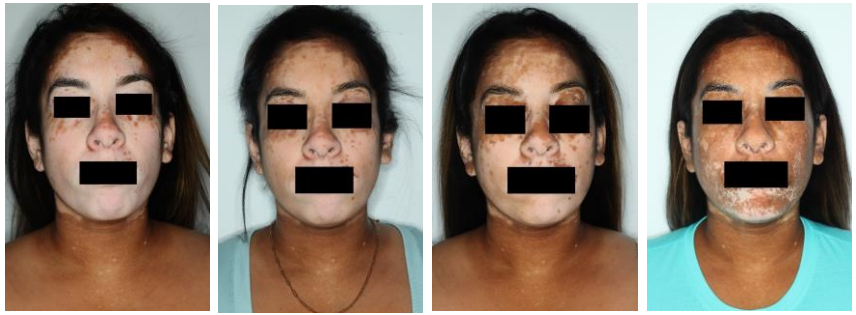
- More patients who received povorcitinib achieved F-VASI75 vs placebo at Week 24 and continued to improve through Week 36 of treatment



Patient Photographs

Patient 1

Baseline	Week 12	Week 24	Week 36
	Povorcitinib 15 mg		Povorcitinib 75 mg

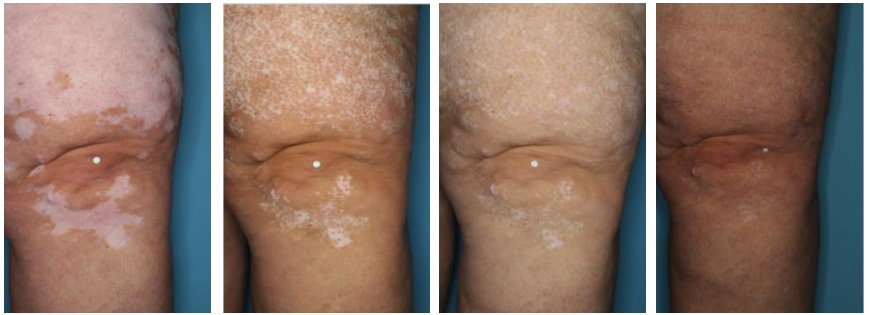


F-VASI percentage change from baseline:

–16.7	–44.4	–85.2

Patient 2

Baseline	Week 12	Week 24	Week 36
	Povorcitinib 15 mg		Povorcitinib 75 mg



T-VASI percentage change from baseline:

–14.6	–31.8	–64.8

Safety

TEAEs in Placebo-Controlled Period (Week 24)

- Oral povorcitinib was generally well tolerated, and no serious TEAEs were considered related to treatment; no new safety signals were observed after Week 24

		Povorcitinib			
	Placebo (n=42)	**15 mg (n=43)**	**45 mg (n=41)**	**75 mg (n=42)**	**Total (n=126)**
Patients with TEAE, n (%)	24 (57.1)	29 (67.4)	30 (73.2)	35 (83.3)	94 (74.6)
Most common TEAEs, n (%)					
COVID-19	5 (11.9)	8 (18.6)	8 (19.5)	5 (11.9)	21 (16.7)
Headache	5 (11.9)	7 (16.3)	1 (2.4)	5 (11.9)	13 (10.3)
Fatigue	2 (4.8)	3 (7.0)	3 (7.3)	6 (14.3)	12 (9.5)
Blood creatine phosphokinase increased	3 (7.1)	3 (7.0)	3 (7.3)	4 (9.5)	10 (7.9)
Acne	0	0	3 (7.3)	6 (14.3)	9 (7.1)
Grade 3 TEAE, n (%)	4 (9.5)	3 (7.0)	5 (12.2)	5 (11.9)	13 (10.3)
TEAE leading to discontinuation, n (%)	2 (4.8)	2 (4.7)	2 (4.9)	3 (7.1)	7 (5.6)
Serious TEAE, n (%)	1 (2.4)	0	1 (2.4)	1 (2.4)	2 (1.6)
Fatal TEAE, n (%)	0	0	0	0	0

Conclusions

- This is the first report of povorcitinib, an oral selective JAK1 inhibitor, in patients with extensive nonsegmental vitiligo
- Povorcitinib was associated with substantial repigmentation in patients with extensive nonsegmental vitiligo after 24 weeks of once-daily treatment
- Continued improvement was seen through 36 weeks of treatment with povorcitinib during the extension period
- All doses of povorcitinib were generally well tolerated, with a favorable safety profile; there were few grade ≥3 or serious TEAEs