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Efficacy and Safety of Oral Povorcitinib in Patients With Prurigo Nodularis: Results From a Randomized, Double-Blind, Placebo-Controlled Phase 2 Study

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Presenting Author Disclosures

- Received honoraria as a speaker and/or consultant for AbbVie, ALK-Abello, Amgen, AstraZeneca, Argenx, Bayer, Beiersdorf, Celldex, Celltrion, Escient, Galderma, GlaxoSmithKline, Incyte Corporation, Jasper, Novartis, Pharvaris, Pfizer, Regeneron, Sanofi, Teva, ThirdHarmonicBio, and Vifor Pharma

Background

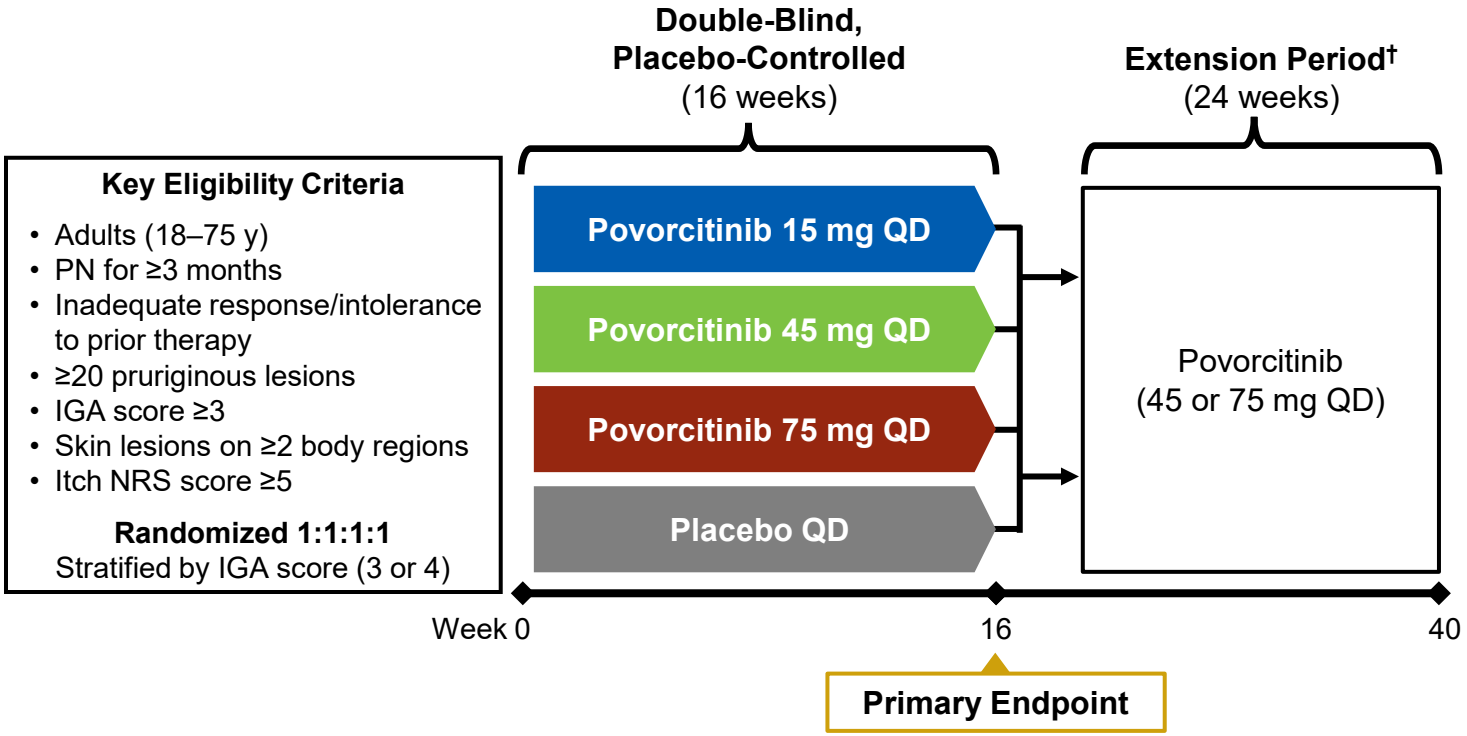
- PN is an inflammatory skin disease characterized by intensely pruritic lesions[1]
- Pathogenesis of PN has been linked to proinflammatory cytokines and chemokines that signal through the JAK/STAT pathway[2,3]
- Povorcitinib is an orally administered, small-molecule selective JAK1 inhibitor[4]

- **Objective:** To assess the efficacy and safety of povorcitinib for the treatment of PN during 16 weeks of treatment

JAK, Janus kinase; PN, prurigo nodularis; STAT, signal transducer and activator of transcription.

1. Aggarwal P, et al. *Clin Exp Dermatol.* 2021;46(7):1277-1284. 2. Agrawal D, et al. *J Cosmet Dermatol.* 2022;21(9):4009-4015. 3. Fukushi S, et al. *Br J Dermatol.* 2011;165(5):990-996. 4. Alavi A, et al. *Br J Dermatol*. 2022;186(5):803-813.

Study Design



IGA, Investigator's Global Assessment; NRS, numerical rating scale; QD, once daily.
ClinicalTrials.gov: NCT05061693; EudraCT: 2021-006329-23.
† Patients in the extension period receive 1 of 2 doses based on their Week 16 responder status.

Assessments

Primary endpoint

- Proportion of patients achieving ≥4-point improvement from baseline in Itch NRS (NRS4[†]) at Week 16

Additional endpoints

- Time to Itch NRS4
- Proportion of patients achieving IGA[‡] treatment success (IGA-TS; IGA score of 0 or 1 with ≥2-grade improvement from baseline) at Week 16
- Proportion of patients achieving both Itch NRS4 and IGA-TS
- Frequency and severity of adverse events

Statistical analysis

- Analysis of the primary endpoint was performed using exact logistic regression
- Secondary endpoints were summarized using descriptive statistics
- Patients with missing data or those who received rescue therapy were imputed as nonresponders

[†] Data for study visits calculated as the average of the prior 7 daily worst itch scores.
[‡] Overall severity rating on a scale from 0 to 4, accounting for the number of pruriginous lesions (score of 0, no pruriginous lesions; score of 1, 1–5 pruriginous lesions).

Patient Demographics and Baseline Clinical Characteristics

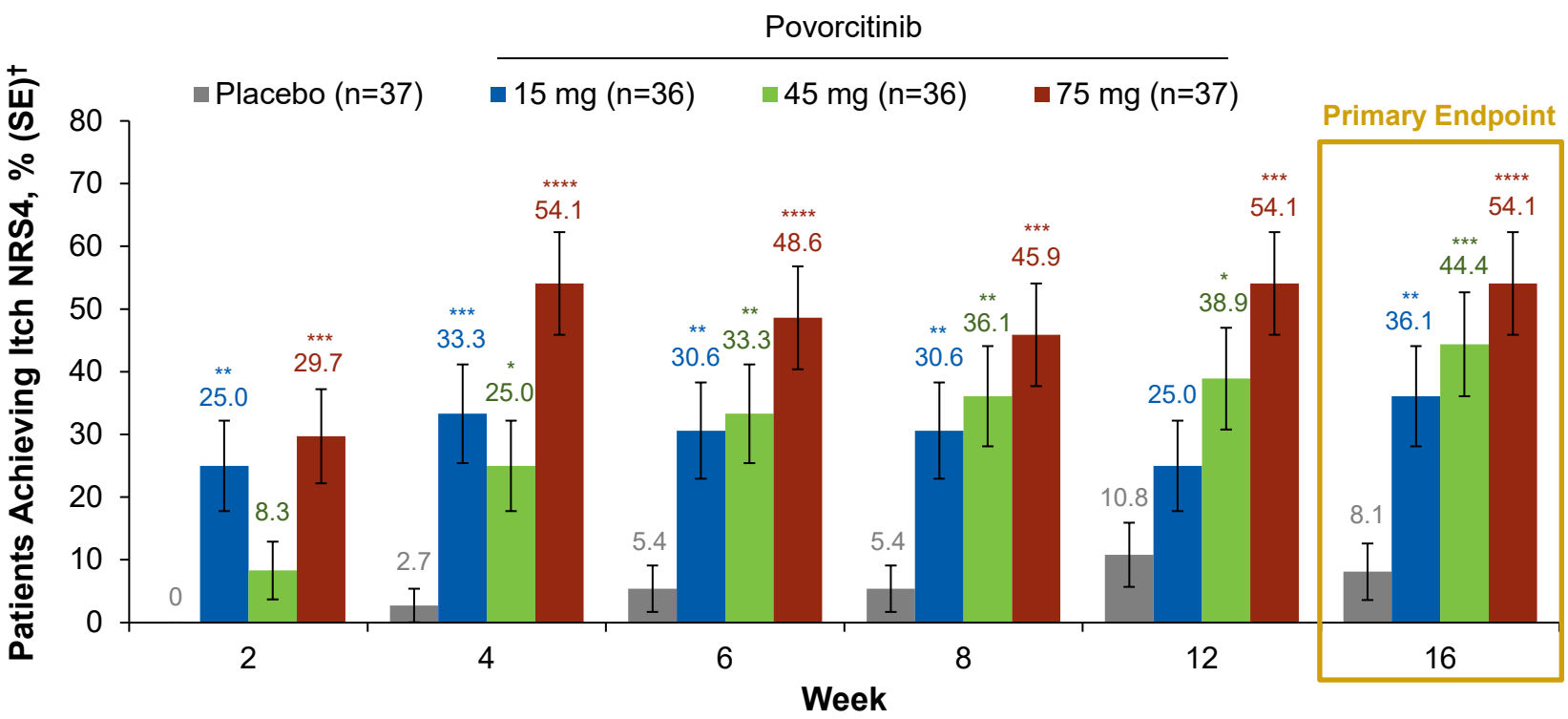
- Patient demographics and baseline clinical characteristics were similar across treatment groups

Characteristic	Overall Population (N=146)
Age, median (range), y	56.0 (19–74)
Female, n (%)	96 (65.8)
White, n (%)	121 (82.9)
BMI, mean (SD), kg/m^2	31.5 (7.2)
Relevant medical history, n (%)	
Depression	36 (24.7)
Seasonal allergy	23 (15.8)
Atopic dermatitis	21 (14.4)
Anxiety	20 (13.7)
Asthma	19 (13.0)
Hypothyroidism	18 (12.3)
Disease duration, median (range), y	4.1 (0.3–31.8)

Characteristic	Overall Population (N=146)
IGA score, n (%)	
3	117 (80.1)
4	28 (19.2)
Itch NRS, mean (SD)	8.0 (1.4)
Itch NRS ≥7.0, n (%)	107 (73.3)
Skin pain NRS, mean (SD)	7.0 (2.2)
DLQI, mean (SD)	15.6 (6.7)
Prior therapy,† n (%)	
Topical corticosteroids	126 (86.3)
Nonsedating antihistamines	50 (34.2)
Sedating antihistamines	25 (17.1)
Oral corticosteroids	21 (14.4)
NB-UVB phototherapy	21 (14.4)

BMI, body mass index; DLQI, Dermatology Life Quality Index; NB-UVB, narrow-band ultraviolet-B.
† Occurring in >10% of patients; patients could receive >1 prior therapy.

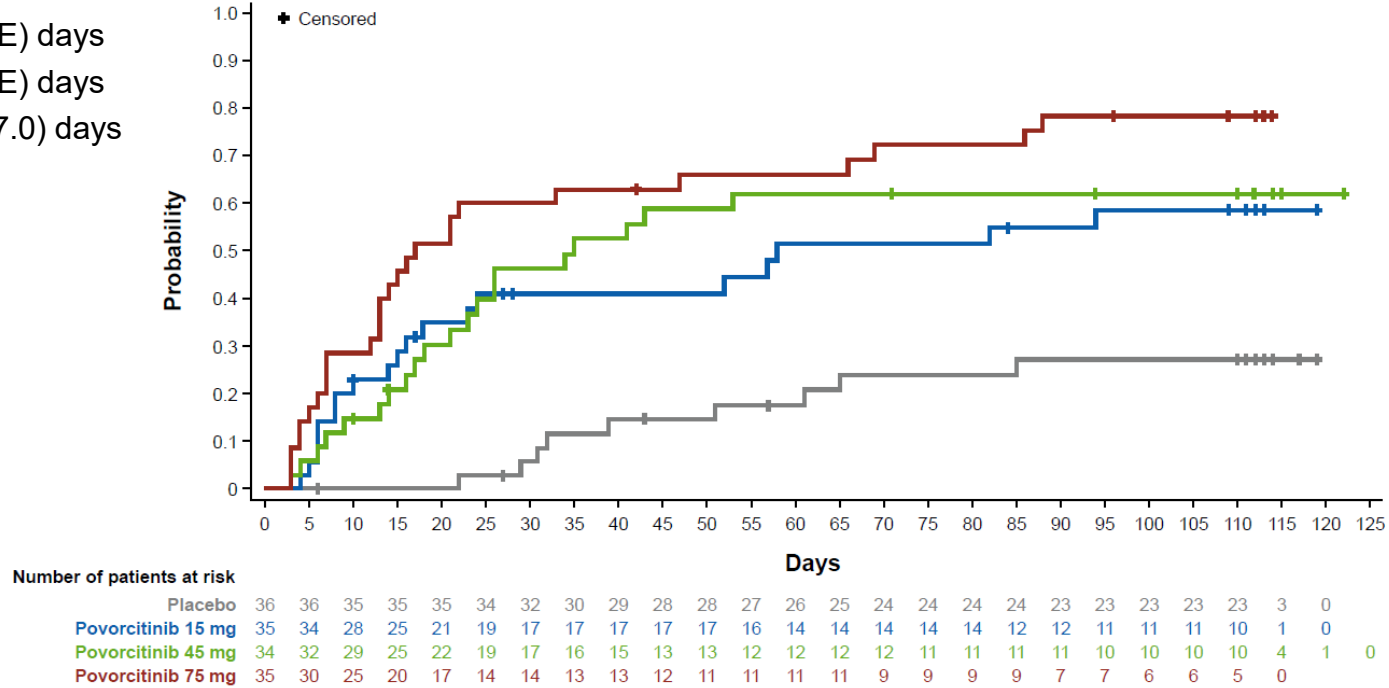
Itch NRS4 Through Week 16



* $P<0.05$ vs placebo; ** $P<0.01$ vs placebo; *** $P<0.001$ vs placebo; **** $P<0.0001$ vs placebo.
† Patients with missing postbaseline data or use of rescue therapy were imputed as nonresponders.
P value calculated for odds ratio of active treatment vs placebo in the intent-to-treat population.

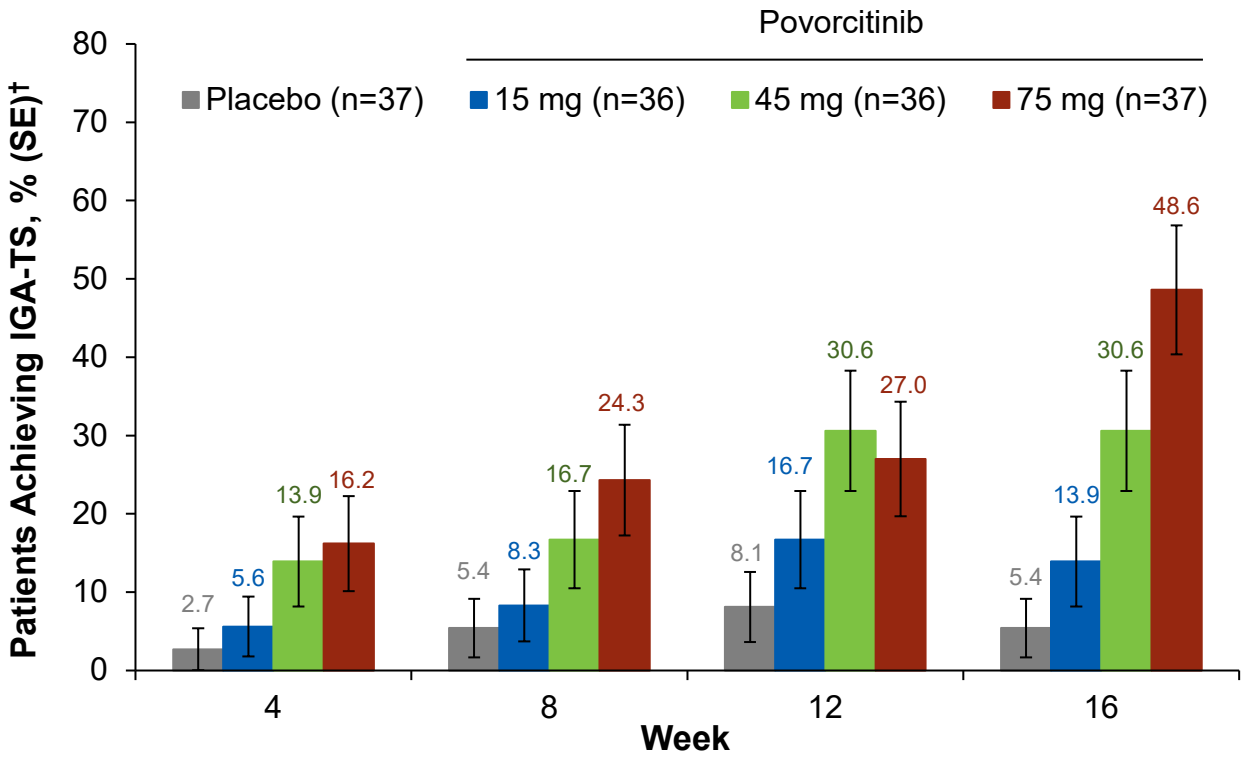
Time to Itch NRS4

- Median (95% CI) times to Itch NRS4 were
  - Placebo: NE
  - 15 mg: 58.0 (16.0–NE) days
  - 45 mg: 35.0 (21.0–NE) days
  - 75 mg: 17.0 (13.0–47.0) days



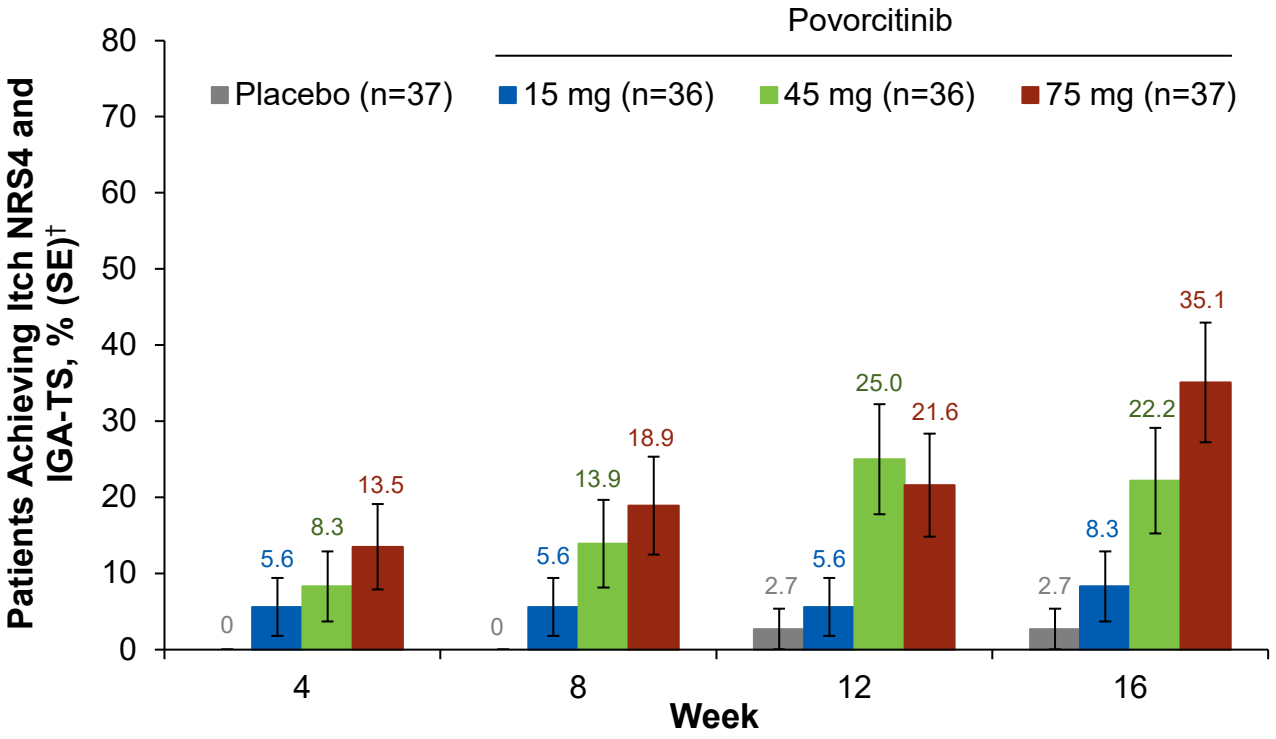
NE, not estimable.

IGA-TS† Through Week 16



† IGA score of 0 (no pruriginous lesion) or 1 (1–5 pruriginous lesions) with ≥2-grade improvement from baseline. Patients with missing postbaseline data or use of rescue therapy were imputed as nonresponders. IGA was not assessed at Weeks 2 and 6 (remote visits).

Itch NRS4 and IGA-TS Through Week 16



† Patients with missing postbaseline data or use of rescue therapy were imputed as nonresponders. IGA was not assessed at Weeks 2 and 6 (remote visits).

Safety at Week 16

- Povorcitinib was generally well tolerated

n (%)	Placebo (n=37)	Povorcitinib 15 mg (n=36)	Povorcitinib 45 mg (n=35)	Povorcitinib 75 mg (n=37)	Povorcitinib Total (n=108)
Patients with TEAE	19 (51.4)	20 (55.6)	25 (71.4)	28 (75.7)	73 (67.6)
Most common TEAEs†					
Headache	0	6 (16.7)	6 (17.1)	0	12 (11.1)
Fatigue	1 (2.7)	5 (13.9)	3 (8.6)	2 (5.4)	10 (9.3)
Nasopharyngitis	3 (8.1)	1 (2.8)	2 (5.7)	5 (13.5)	8 (7.4)
Patients with serious TEAE	1 (2.7)	2 (5.6)	4 (11.4)	3 (8.1)	9 (8.3)
Patients with grade ≥3 TEAE	0	1 (2.8)	1 (2.9)	2 (5.4)	4 (3.7)
Patients with TEAE leading to discontinuation	1 (2.7)	3 (8.3)	2 (5.7)	0	5 (4.6)

- 1 patient died in the 15-mg povorcitinib group (Day 9 of exposure; considered not related)
  - 70-year-old woman, BMI 49 kg/m^2, previous smoker
  - Relevant medical history included COPD and high blood pressure

COPD, chronic obstructive pulmonary disorder; TEAE, treatment-emergent adverse event.
† Occurring in >6% of patients in the total povorcitinib group.

Conclusions

- Once-daily povorcitinib had a meaningful (≥4-point reduction in Itch NRS4) and early impact on itch
- More patients receiving povorcitinib achieved IGA-TS or combined IGA-TS and Itch NRS4 compared with placebo
- Povorcitinib was generally well tolerated with no new safety concerns identified
- These phase 2 study results suggest povorcitinib is a promising, potential novel treatment for PN

Thank You

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

- For questions, please contact Prof Martin Metz (martin.metz@charite.de)

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