Presentation #D2T01.3F

Efficacy and Safety of Oral Povorcitinib in Patients With Prurigo Nodularis: 40-Week Results From a Randomized, Double-Blind, Placebo-Controlled Phase 2 Study

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Presenting Author Disclosures

- Shawn G. Kwatra has served as a consultant for AbbVie, Amgen, Celldex, Galderma, Incyte Corporation, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi
- Received grants/research funding from Galderma, Incyte Corporation, Pfizer, and Sanofi

Introduction

- PN is a chronic inflammatory skin disease characterized by intensely pruritic lesions resulting from chronic scratching[1,2]
- Pathogenesis involves multiple immune axes, including Th1, Th2, Th17, and Th22[3]
- Povorcitinib is an oral, small-molecule, selective JAK1 inhibitor[4]
- Povorcitinib was associated with an early improvement in itch, a meaningful impact on IGA, and was generally well tolerated in a 16-week randomized, placebo-controlled, phase 2 dose-ranging study[5]

Objective:
To assess the longer-term efficacy and safety of response-based povorcitinib dosing in patients with PN from the phase 2 dose-ranging study following 40 weeks of treatment

IGA, Investigator's Global Assessment; JAK, Janus kinase; PN, prurigo nodularis.

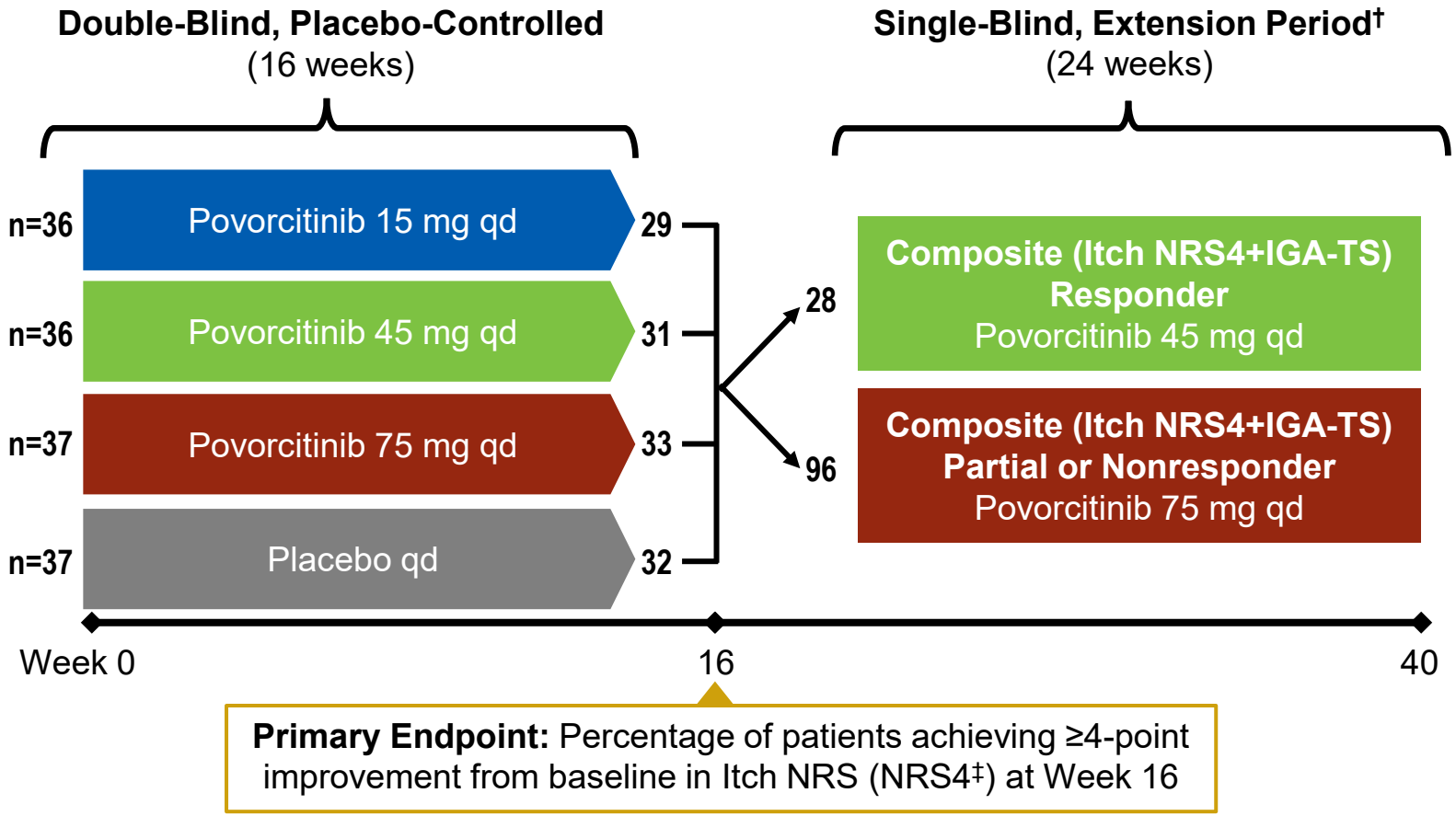
1. Aggarwal P, et al. *Clin Exp Dermatol*. 2021;46(7):1277-1284. 2. Agrawal D, et al. *Indian J Dermatol*. 2021;66(6):638-644. 3. Belzberg M, et al. *J Invest Dermatol*. 2021;141(9):2208-2218. 4. Alavi A, et al. *Br J Dermatol*. 2022;186(5):803-813. 5. Kwatra SG, et al. Presented at: American Academy of Dermatology Annual Meeting; March 8–12, 2024; San Diego, CA.

Study Design (NCT05061693; EudraCT 2021-006329-23)

Key Eligibility Criteria

- Adults (18–75 y)
- PN for ≥3 months
- ≥20 pruriginous lesions on ≥2 body regions
- IGA score ≥3
- Itch NRS score ≥5
- Inadequate response/ intolerance to prior therapy

Randomized 1:1:1:1
Stratified by IGA score (3 or 4)



IGA, Investigator's Global Assessment; IGA-TS, IGA treatment success (score of 0 [no pruriginous lesion] or 1 [1–5 pruriginous lesions] with ≥2-grade improvement from baseline); NRS, numerical rating scale; PN, prurigo nodularis; qd, once daily.
† Patients who achieved both Itch NRS4 and IGA-TS (composite response) without any missing data or needing rescue therapy during the placebo-controlled period were considered as responders. Patients not meeting the definition of a responder were considered as nonresponders. ‡ Data for study visits calculated as the average of the prior 7 daily worst itch scores.

Patient Demographics and Baseline Clinical Characteristics

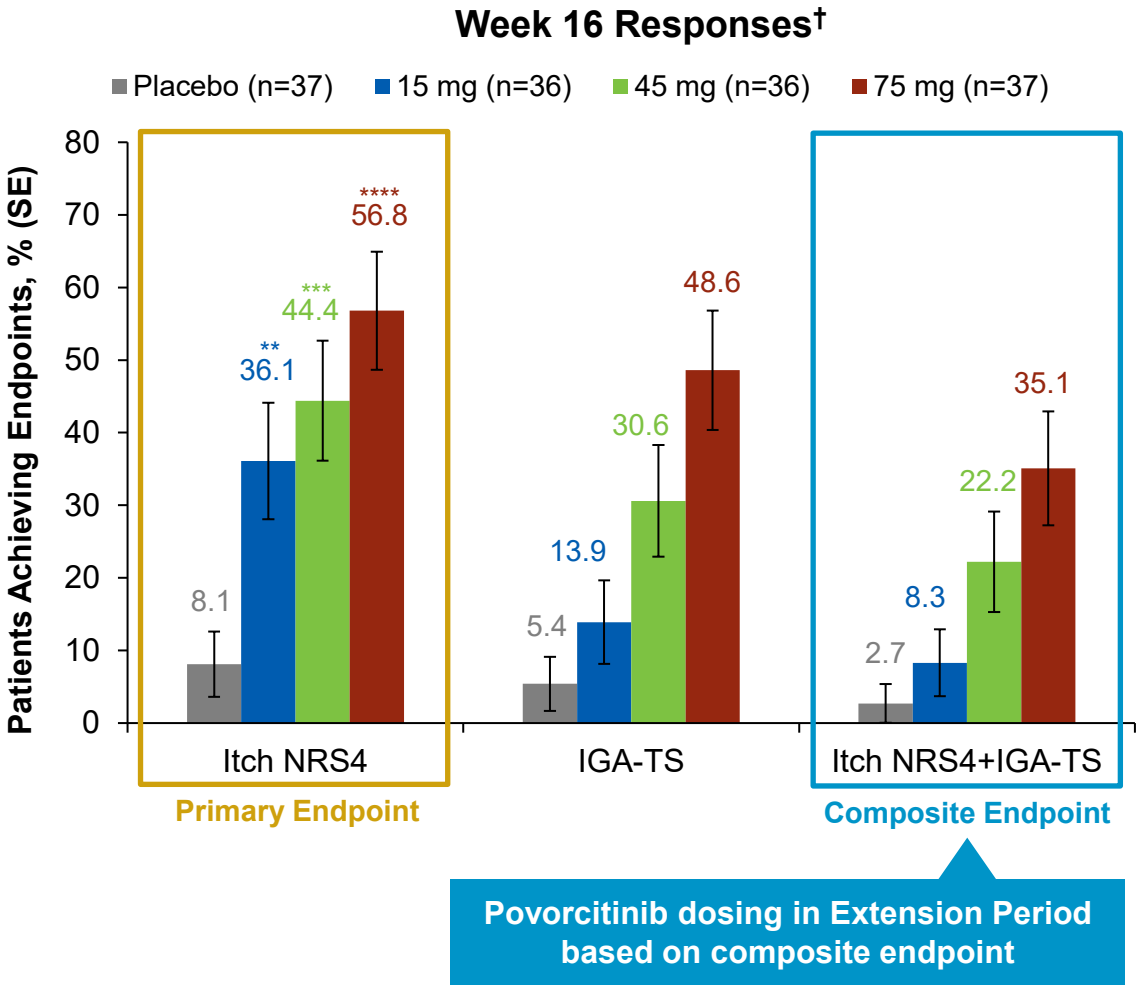
- Patient demographics and baseline clinical characteristics were similar across treatment groups

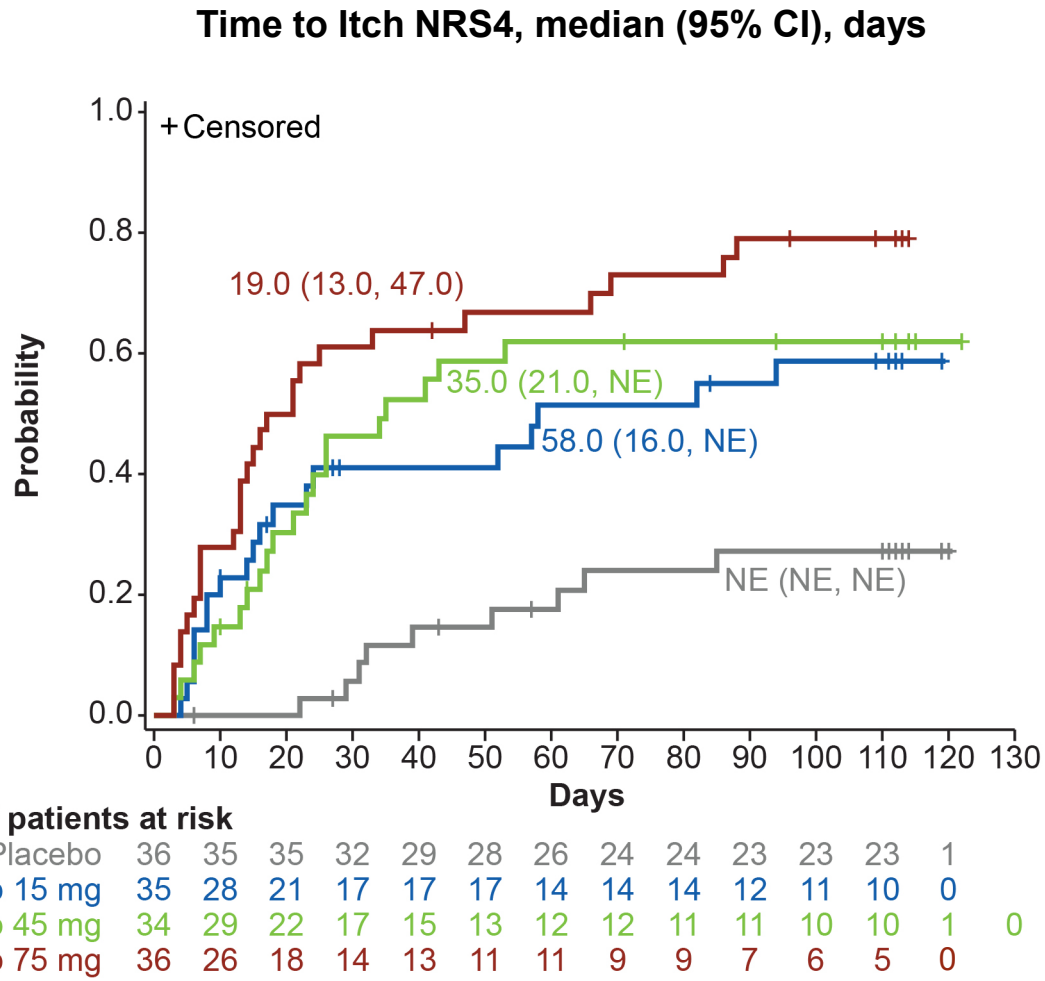
Characteristic	Overall Population (N=146)
Age, median (range), y	56.0 (19–74)
Female, n (%)	96 (65.8)
White, n (%)	121 (82.9)
BMI, mean (SD), kg/m^2	31.5 (7.2)
Relevant medical history, n (%)	
Depression	36 (24.7)
Seasonal allergy	23 (15.8)
Atopic dermatitis	21 (14.4)
Anxiety	20 (13.7)
Asthma	19 (13.0)
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	29 (19.9)
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	52 (35.6)
Sedating antihistamines	25 (17.1)
Oral corticosteroids	21 (14.4)
NB-UVB phototherapy	22 (15.1)

BMI, body mass index; DLQI, Dermatology Life Quality Index; IGA, Investigator's Global Assessment; NB-UVB, narrow-band ultraviolet-B; NRS, numerical rating scale.
* Data missing for one patient. † Occurring in >10% of patients; patients could receive >1 prior therapy.

Week 16 Responses (ITT Population, NRI)





Number of patients at risk

Placebo	36	35	35	32	29	28	26	24	24	23	23	23	1
Povorcitinib 15 mg	35	28	21	17	17	17	14	14	14	12	11	10	0
Povorcitinib 45 mg	34	29	22	17	15	13	12	12	11	11	10	10	1	0
Povorcitinib 75 mg	36	26	18	14	13	11	11	9	9	7	6	5	0

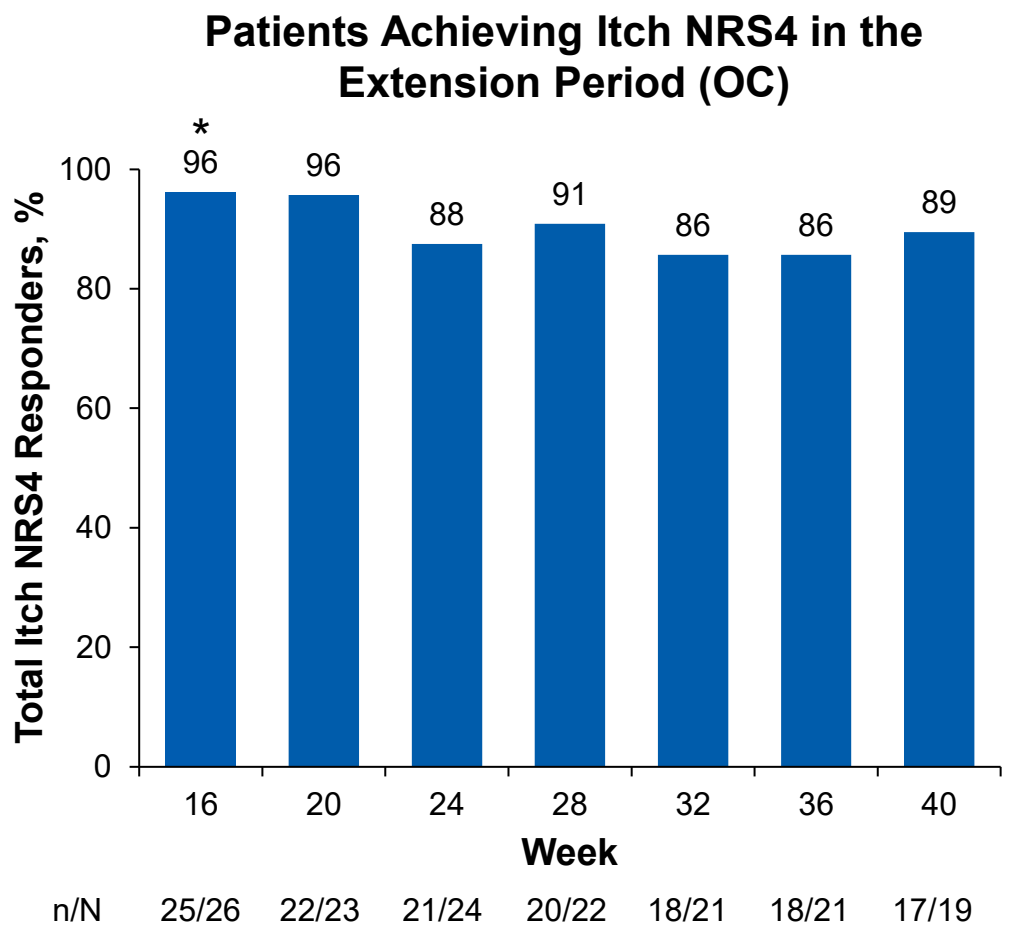
IGA-TS, Investigator's Global Assessment treatment success; ITT, intent-to-treat; NRI, nonresponder imputation; NRS4, ≥4-point improvement from baseline in Itch numerical rating scale.

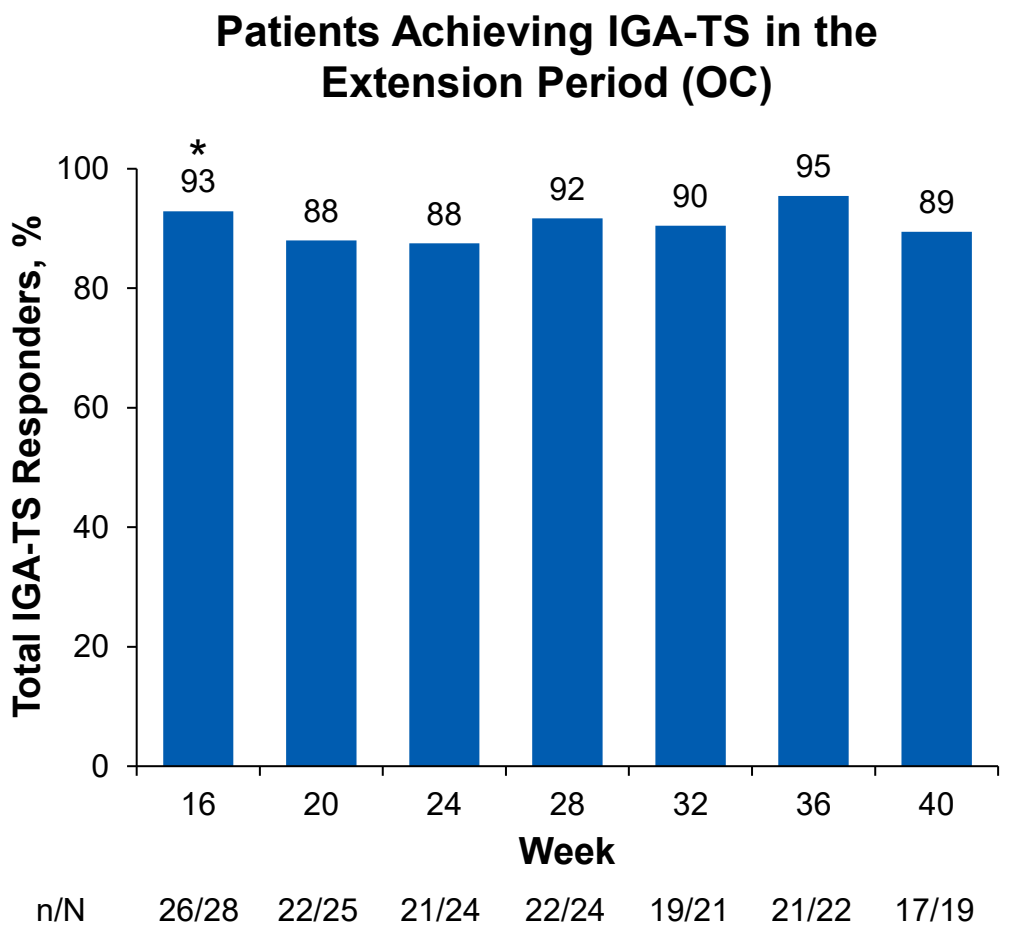
** *P*<0.01, *** *P*<0.001, **** *P*<0.0001 vs placebo. *P* value was calculated for odds ratio of active treatment vs placebo in the ITT population.

† Patients with missing postbaseline data or use of rescue therapy were imputed as nonresponders.

Itch NRS4 and IGA-TS Responses With Povorcitinib 45 mg

In Week 16 Composite Responders



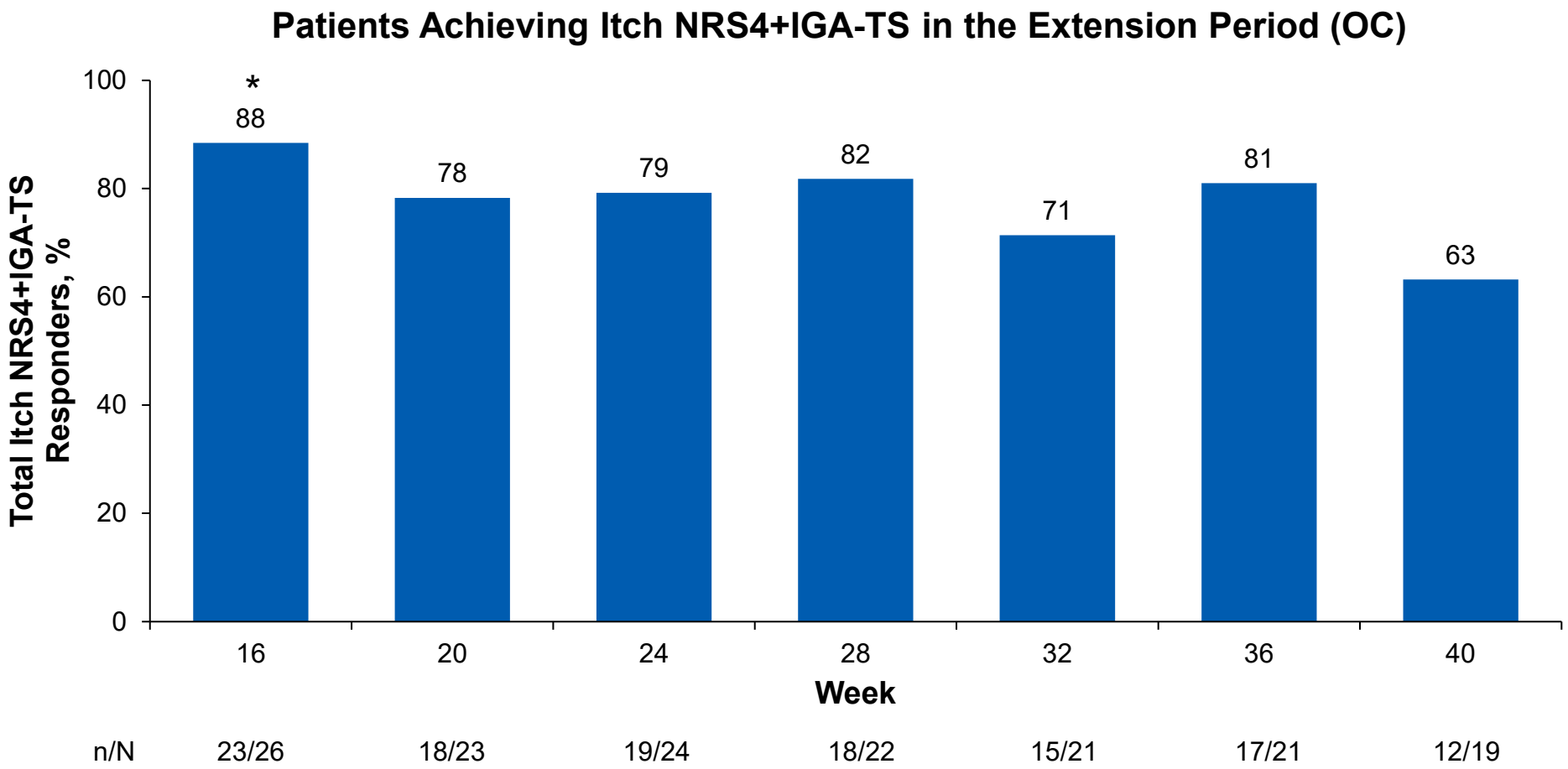


IGA-TS, Investigator's Global Assessment treatment success (score of 0 [no pruriginous lesion] or 1 [1–5 pruriginous lesions] with ≥2-grade improvement from baseline); NRS4, ≥4-point improvement from baseline in Itch numerical rating scale; OC, observed cases.

* 5 patients were designated Week 16 composite responders who did not meet full criteria.

Composite Responses With Povorcitinib 45 mg

In Week 16 Composite Responders



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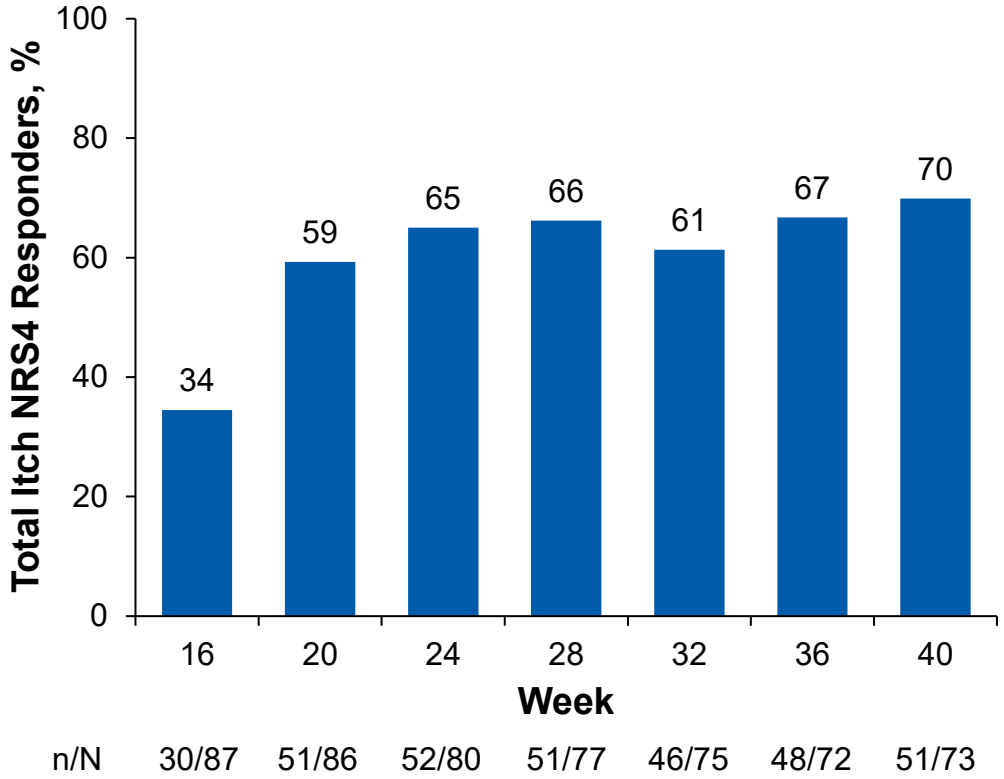
* 5 patients were designated Week 16 composite responders who did not meet full criteria.

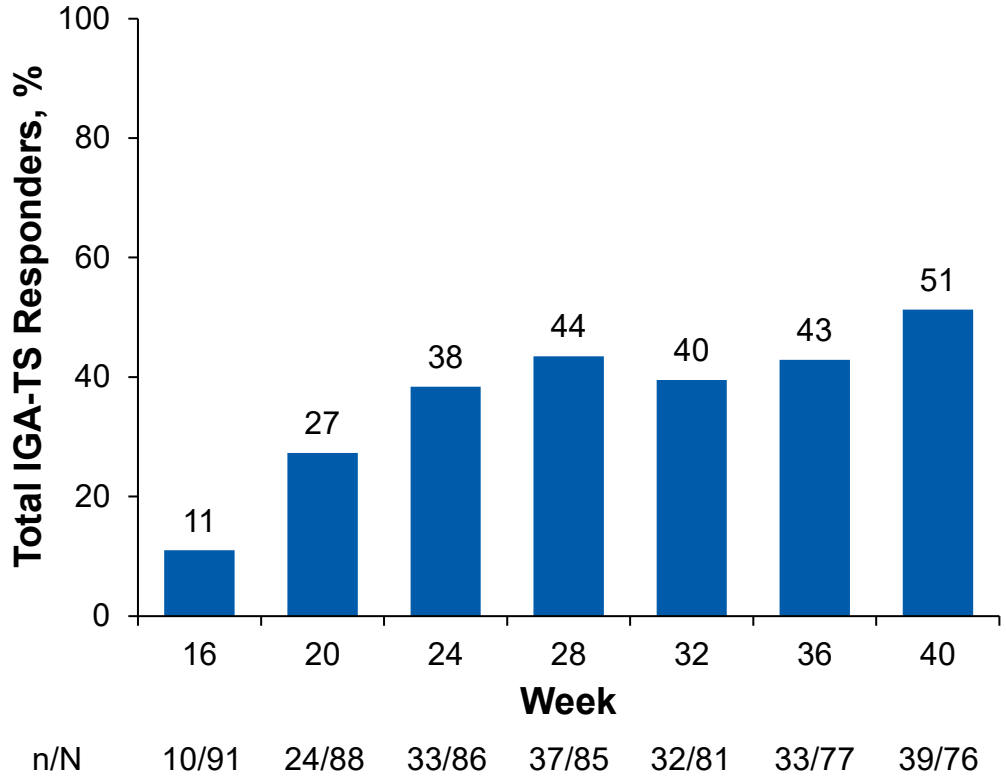
Itch NRS4 and IGA-TS Responses With Povorcitinib 75 mg

In Week 16 Composite Nonresponders

Patients Achieving Itch NRS4 in the Extension Period (OC)



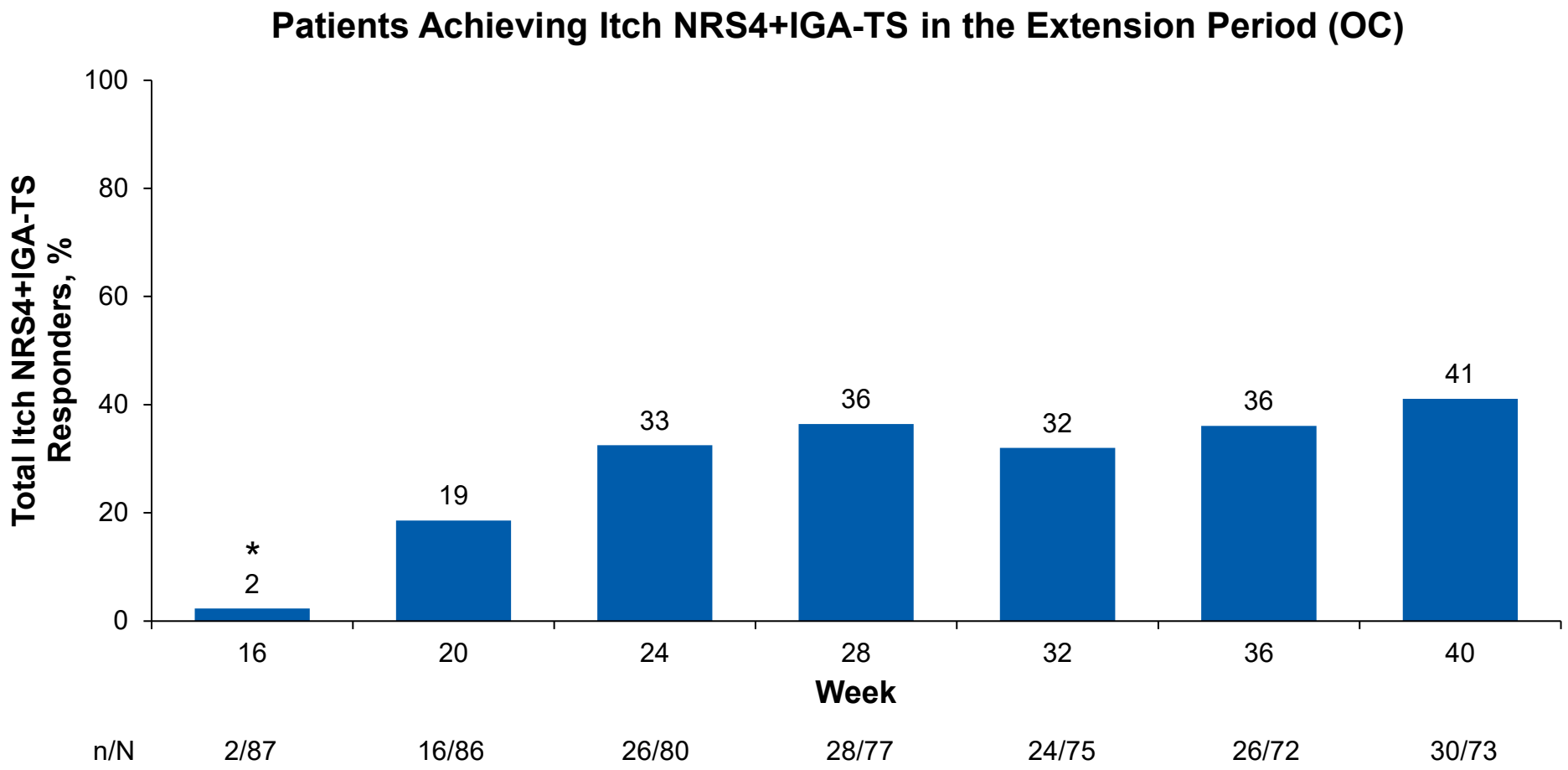
Patients Achieving IGA-TS in the Extension Period (OC)



IGA-TS, Investigator's Global Assessment treatment success (score of 0 [no pruriginous lesion] or 1 [1–5 pruriginous lesions] with ≥2-grade improvement from baseline); NRS4, ≥4-point improvement from baseline in Itch numerical rating scale; OC, observed cases.

Composite Responses With Povorcitinib 75 mg

In Week 16 Composite Nonresponders



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* 2 patients were designated Week 16 nonresponders who did not meet full criteria.

Safety During the Extension Period (Week 16–40)

Patients, n (%)	Week 16 Responders Povorcitinib 45 mg (n=28)	Week 16 Nonresponders Povorcitinib 75 mg (n=96)
Any TEAE	15 (53.6)	68 (70.8)
Grade ≥3 TEAE	1 (3.6)	7 (7.3)
SAE	1 (3.6)	6 (6.3)
Fatal	0	0
TEAE leading to discontinuation	2 (7.1)	6 (6.3)
Treatment-related TEAE	8 (28.6)	23 (24.0)
Treatment-related SAE	0	0
Treatment-related grade ≥3 TEAE	0	0
Most common TEAEs†		
Nasopharyngitis	3 (10.7)	6 (6.3)
COVID-19	2 (7.1)	6 (6.3)
Diarrhea	2 (7.1)	1 (1.0)
Epistaxis	2 (7.1)	2 (2.1)
Fatigue	2 (7.1)	3 (3.1)
Neurodermatitis	2 (7.1)	7 (7.3)
Weight increased	2 (7.1)	5 (5.2)
Hemoglobin decreased	0	9 (9.4)
Blood CPK increased	1 (3.6)	7 (7.3)
Back pain	0	5 (5.2)

Patients, n (%)	Week 16 Responders Povorcitinib 45 mg (n=28)	Week 16 Nonresponders Povorcitinib 75 mg (n=96)
Anemia	0	3 (3.1)
Infections		
Grade ≥3‡	0	5 (5.2)
Leading to discontinuation§	0	1 (1.0)
Herpes zoster	0	0
Upper respiratory tract infection	1 (3.6)	3 (3.1)
Urinary tract infection	1 (3.6)	3 (3.1)

CPK, creatine phosphokinase; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
† Occurring in >5% of Week 16 responders or nonresponders. ‡ Grade ≥3 infections included appendicitis, COVID-19, erysipelas, mastitis, and pneumonia (n=1 each).
§ Mastitis led to treatment discontinuation in one patient.

Conclusions

- Once-daily povorcitinib resulted in meaningful and sustained improvements in itch and lesions in patients with recalcitrant PN
  - Observed responses at Week 16 continued with povorcitinib 45 mg in the majority of cases
  - Povorcitinib 75 mg achieved responses in patients who did not respond at lower doses
- Povorcitinib was generally well tolerated with no new safety concerns identified with longer-term treatment
- Povorcitinib is a promising, novel, oral treatment for patients with PN, with the potential for early and long-term disease control
- Future studies will investigate if longer treatment durations with povorcitinib 45 or 75 mg are beneficial for achieving Itch NRS4+IGA-TS composite responses

Thank You For Your Attention

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