Efficacy and Safety of Ruxolitinib Cream in Patients With Prurigo Nodularis: Results From a Phase 3, Randomized, Vehicle-Controlled Study (TRuE-PN1)

Shawn G. Kwatra, MD,[1,2] Stephen K. Tyring, MD, PhD,[3] Alan B. Fleischer Jr., MD,[4] Sue Moran, MSN,[5] Haq Nawaz, MD, MPH, MBA, MS,[5] Kang Sun, PhD,[5] Sonja Ständer, MD[6]

[1]Department of Dermatology, University of Maryland School of Medicine, Baltimore, MD, USA; [2]Maryland Itch Center, University of Maryland School of Medicine, Baltimore, MD, USA; [3]McGovern Medical School, University of Texas Health Science Center, Houston, TX, USA; [4]University of Cincinnati College of Medicine, Cincinnati, OH, USA; [5]Incyte Corporation, Wilmington, DE, USA; [6]Center for Chronic Pruritus, Münster University Hospital, Münster, Germany

American Academy of Dermatology Annual Meeting; March 7–11, 2025; Orlando, Florida

Presenting Author Disclosures

- Shawn G. Kwatra has served as an advisory board member/consultant for AbbVie, Amgen, Arcutis Biotherapeutics, Aslan Pharmaceuticals, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Celldex Therapeutics, Dermavant, Galderma, Genzada Pharmaceuticals, Incyte Corporation, Johnson & Johnson, LEO Pharma, Novartis Pharmaceuticals Corporation, Pfizer, Regeneron Pharmaceuticals, and Sanofi and has served as an investigator for Galderma, Incyte Corporation, Pfizer, and Sanofi

Background

- PN is a chronic inflammatory disease consisting of cutaneous nodules associated with intense itch[1,2]
- Pathogenesis of PN has been linked to proinflammatory cytokines and chemokines (Th1, Th2, Th17, and Th22)[3] that signal through the JAK/STAT pathway[4-6]
- Ruxolitinib cream is a selective JAK1/JAK2 inhibitor designed for topical administration[7,8]

Objective:

To evaluate efficacy and safety of 1.5% ruxolitinib cream BID up to Week 12 in patients with PN from a phase 3, randomized, double-blind, vehicle-controlled study (NCT05755438)

BID, twice daily; JAK, Janus kinase; PN, prurigo nodularis; STAT, signal transducer and activator of transcription; Th, T helper cell.

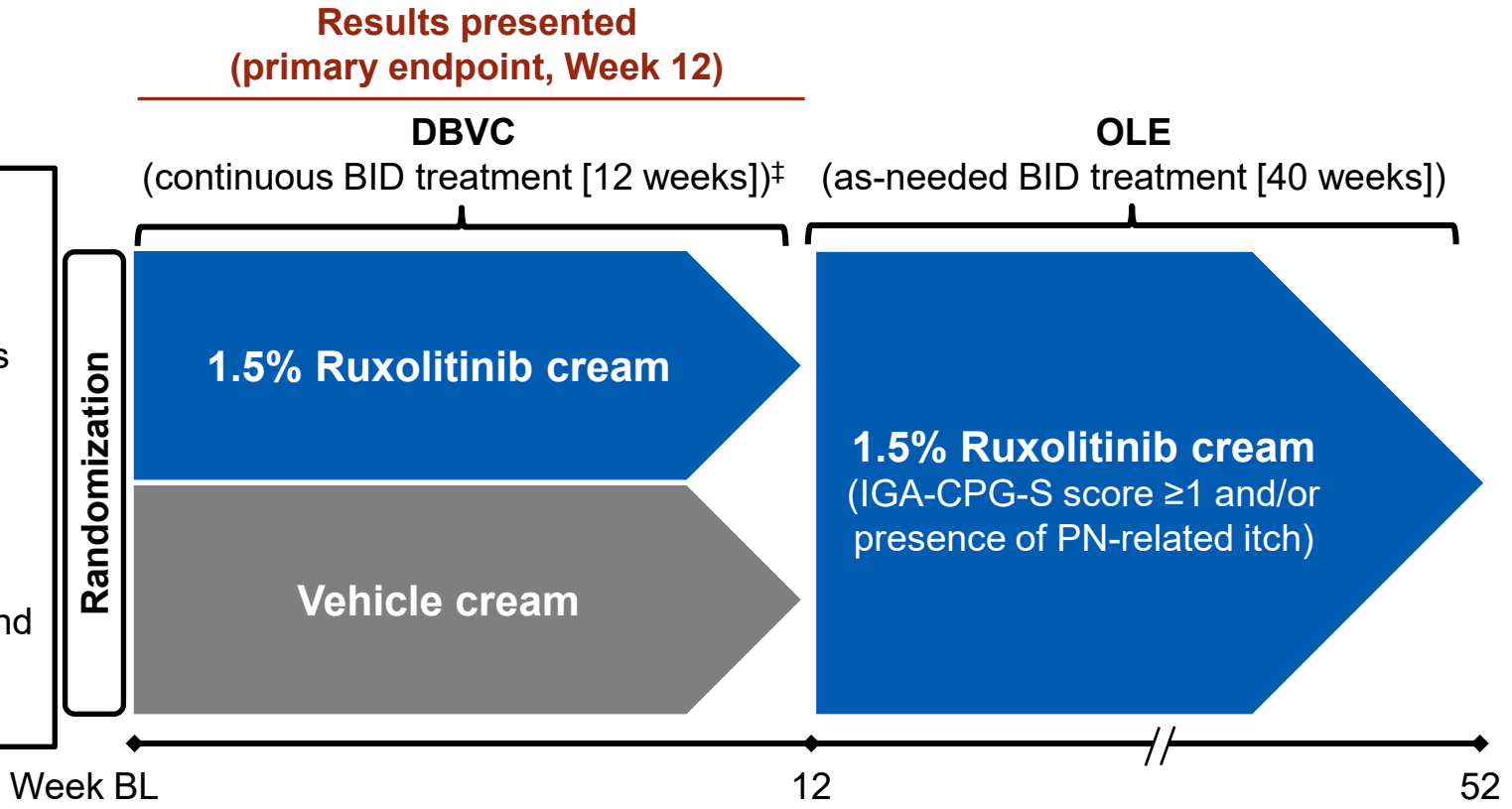
1. Elmariah S, et al. *J Am Acad Dermatol.* 2021;84(3):747-760. 2. Pereira MP, et al. *J Eur Acad Dermatol Venereol.* 2020;34(10):2373-2383. 3. Wong LS, Yen YT. *Int J Mol Sci.* 2022;23(20):12390. 4. Agrawal D, et al. *J Cosmet Dermatol.* 2022;21(9):4009-4015. 5. Fukushi S, et al. *Br J Dermatol.* 2011;165(5):990-996. 6. Howell MD, et al. *Front Immunol.* 2019;10:2342. 7. Quintás-Cardama A, et al. *Blood.* 2010;115(15):3109-3117. 8. Smith P, et al. *Pharmaceutics.* 2021;13(7):1044.

Study Design

Key Eligibility Criteria

- Adults aged ≥18 years
- PN diagnosis ≥3 months
- ≥6 pruriginous lesions on ≥2 different body areas
- IGA-CPG-S score ≥2
- WI-NRS score† ≥7
- Treatment BSA (excluding scalp) ≤20%‡

Randomized 1:1
(Stratified by baseline IGA-CPG-S score [2 or ≥3] and geographic area [North America or outside North America])



Primary endpoint: WI-NRS4 response at Week 12
Key secondary endpoints: WI-NRS4 response at Week 4, overall TS§ at Week 12, IGA-CPG-S-TS at Week 12, WI-NRS4 response at Day 7

BL, baseline; BSA, body surface area; DBVC, double-blind vehicle-controlled; IGA-CPG-S, Investigator's Global Assessment for Stage of Chronic Prurigo; IGA-CPG-S-TS, IGA-CPG-S treatment success (IGA-CPG-S score of 0 or 1 with a ≥2-grade improvement from baseline); OLE, open-label extension; TS, treatment success; WI-NRS, Worst-Itch Numerical Rating Scale; WI-NRS4, ≥4-point improvement from baseline in WI-NRS score.
† Baseline and study visit scores calculated as the average of the 7 prior daily scores (data available for ≥4 days).
‡ During the DBVC period, treatment was applied directly to each pruriginous lesion (including ~1 cm of the surrounding area) identified at baseline as well as new lesions identified postbaseline after consultation with the investigator (≤20% BSA).
§ Overall TS was defined as achievement of WI-NRS4 and IGA-CPG-S-TS.

Patient Demographics and Baseline Clinical Characteristics

ITT Population

Demographics	Vehicle (n=103)	1.5% Ruxolitinib cream (n=101)
Age, median (range), y	63.0 (20–83)	63.0 (20–79)
Female, n (%)	65 (63.1)	64 (63.4)
Race, n (%)		
White	84 (81.6)	87 (86.1)
Black	9 (8.7)	7 (6.9)
Asian and others	9 (8.7)	5 (5.0)
Missing	1 (1.0)	2 (2.0)
Geographical region, n (%)		
North America	49 (47.6)	47 (46.5)
Outside North America	54 (52.4)	54 (53.5)

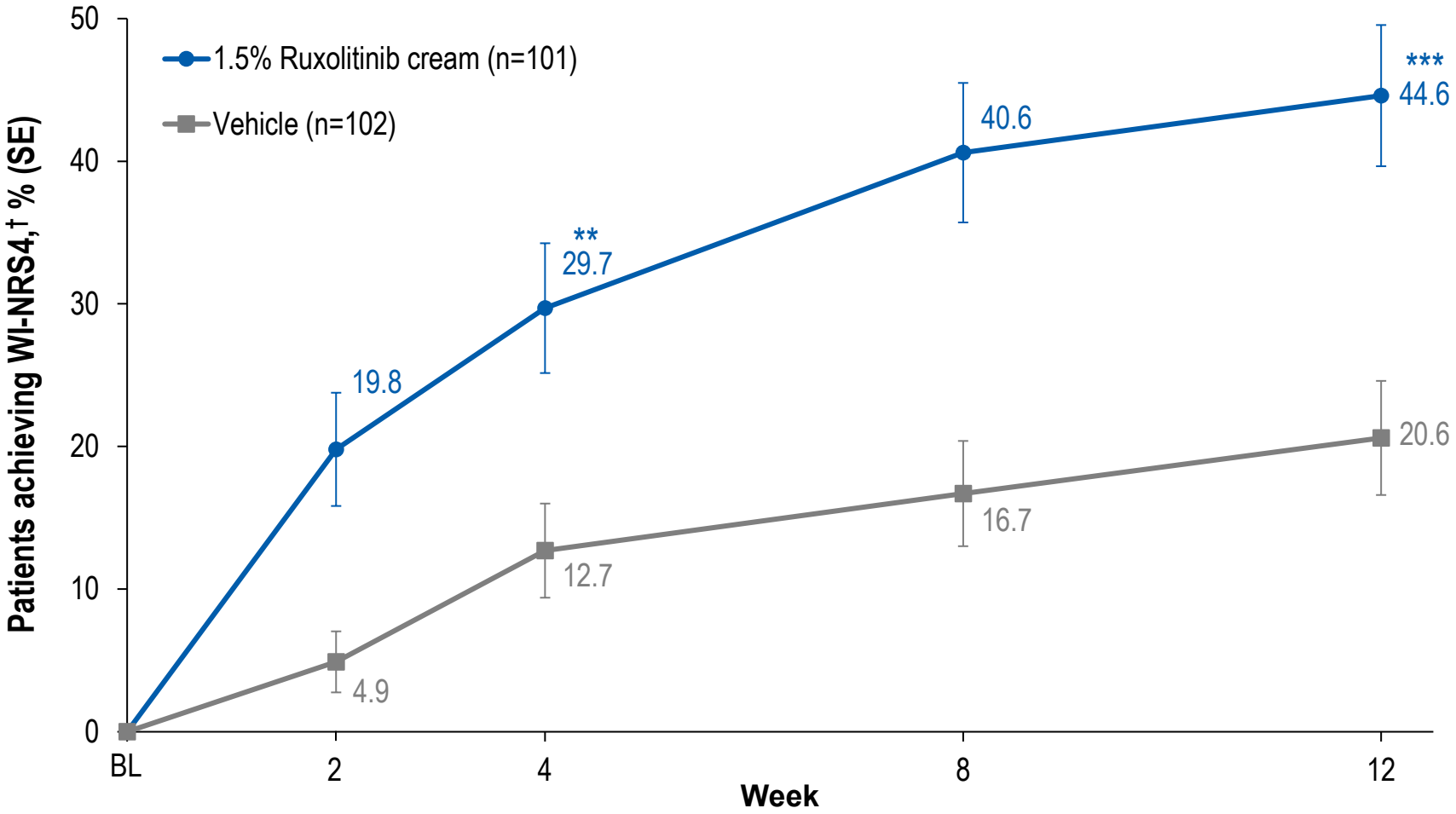
Clinical characteristics	Vehicle (n=103)	1.5% Ruxolitinib cream (n=101)
Disease duration, median (range), y	4.7 (0.3–45.4)	4.1 (0.3–66.8)
WI-NRS score, mean (SD)	8.4 (0.8)	8.4 (1.0)
Skin Pain NRS score, mean (SD)	7.5 (2.0)	7.1 (2.4)
Treatment BSA, mean (SD), %	8.8 (5.4)	8.8 (5.4)
IGA-CPG-S score, n (%)		
2	21 (20.4)	18 (17.8)
≥3	82 (79.6)	83 (82.2)
Prior TCS therapy for PN,† n (%)		
Very potent	29 (28.2)	24 (23.8)
Potent	27 (26.2)	28 (27.7)
Moderately potent	5 (4.9)	11 (10.9)

ITT, intent to treat; NRS, numerical rating scale; TCS, topical corticosteroid.

† Patients could have used >1 therapy and does not include TCS used in combination with other agents.

WI-NRS4 Response by Visit

Nonresponder Imputation



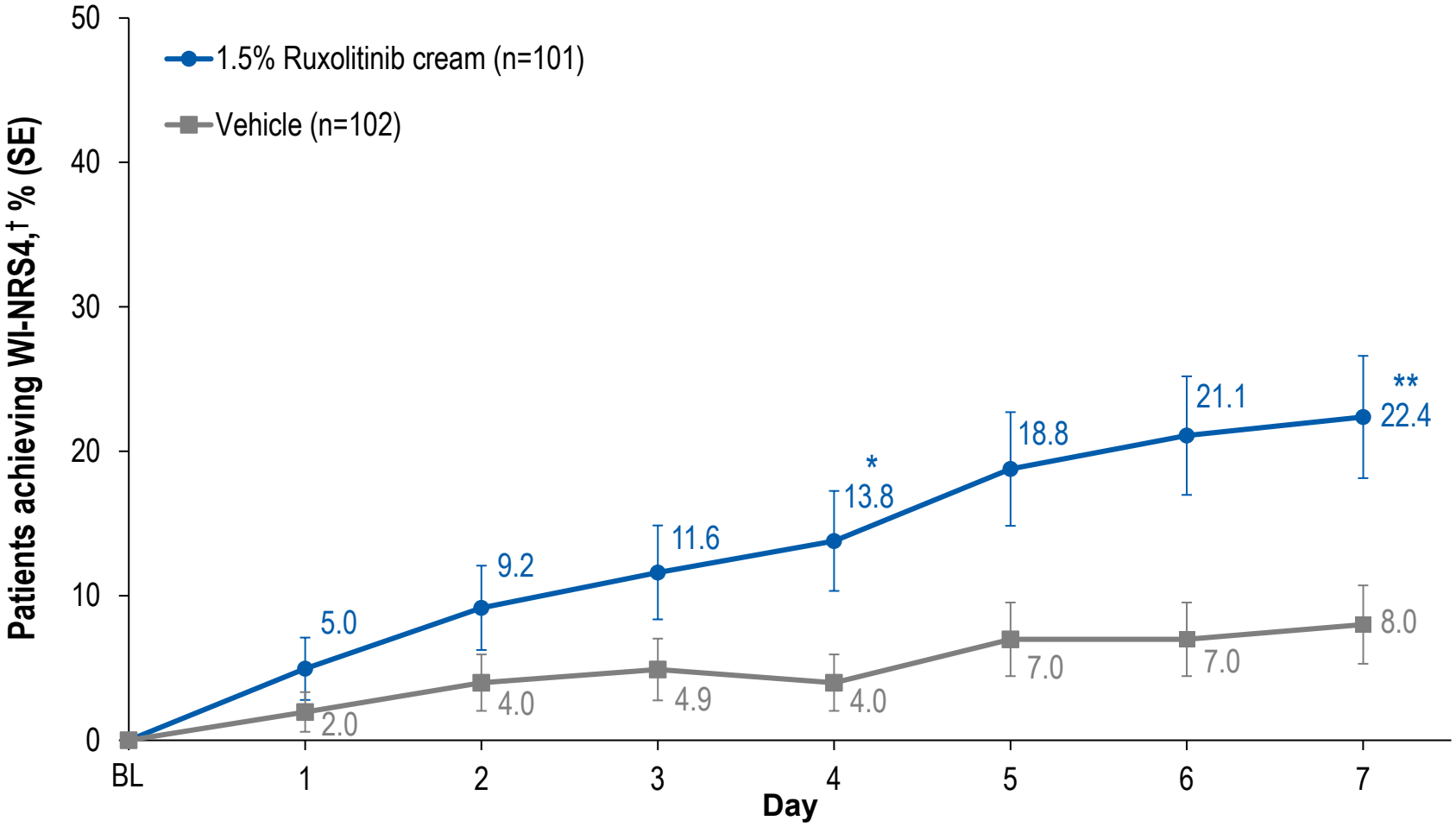
** *P*<0.01 vs vehicle; *** *P*<0.001 vs vehicle.

P values were only assessed at Weeks 4 and 12 (Cochran-Mantel-Haenszel test stratified by baseline IGA-CPG-S score [2 or ≥3] and geographic region [North America or outside of North America]).

† Patients with a WI-NRS score ≥4 at baseline were included in this analysis. Patients with missing data were imputed as nonresponders.

WI-NRS4 Response in the First Week

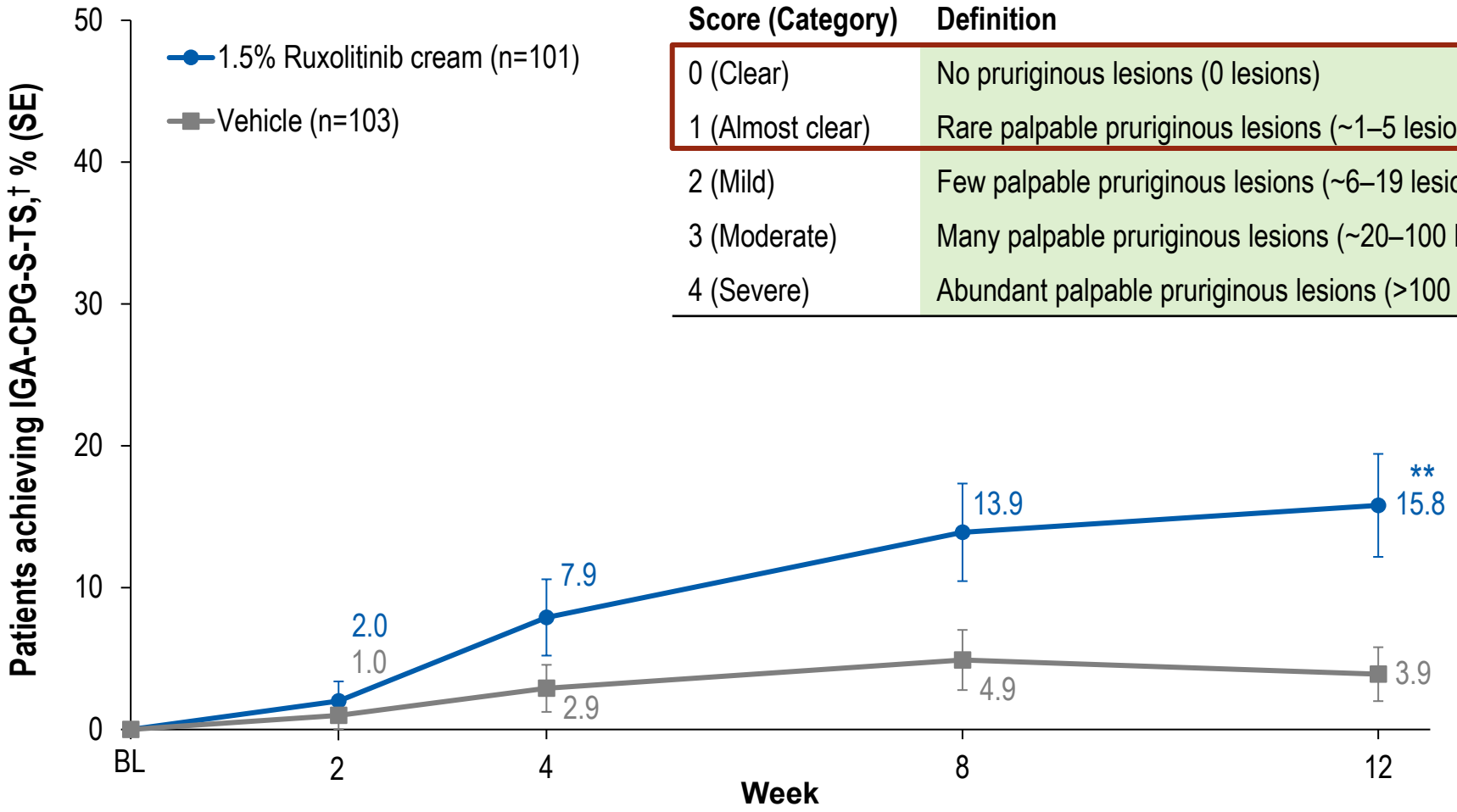
Multiple Imputation



* *P*<0.05 vs vehicle; ** *P*<0.01 vs vehicle.
P value assessment was prespecified at Day 7 (Cochran-Mantel-Haenszel test stratified by baseline IGA-CPG-S score [2 or ≥3] and geographic region [North America or outside of North America]). Day 4 *P* value was a post hoc analysis.
† Patients with a WI-NRS score ≥4 at baseline were included in this analysis. Multiple imputation was used for patients with missing data.

IGA-CPG-S-TS by Visit

Nonresponder Imputation



Score (Category)	Definition
0 (Clear)	No pruriginous lesions (0 lesions)
1 (Almost clear)	Rare palpable pruriginous lesions (~1–5 lesions)
2 (Mild)	Few palpable pruriginous lesions (~6–19 lesions)
3 (Moderate)	Many palpable pruriginous lesions (~20–100 lesions)
4 (Severe)	Abundant palpable pruriginous lesions (>100 lesions)

With ≥2-grade improvement

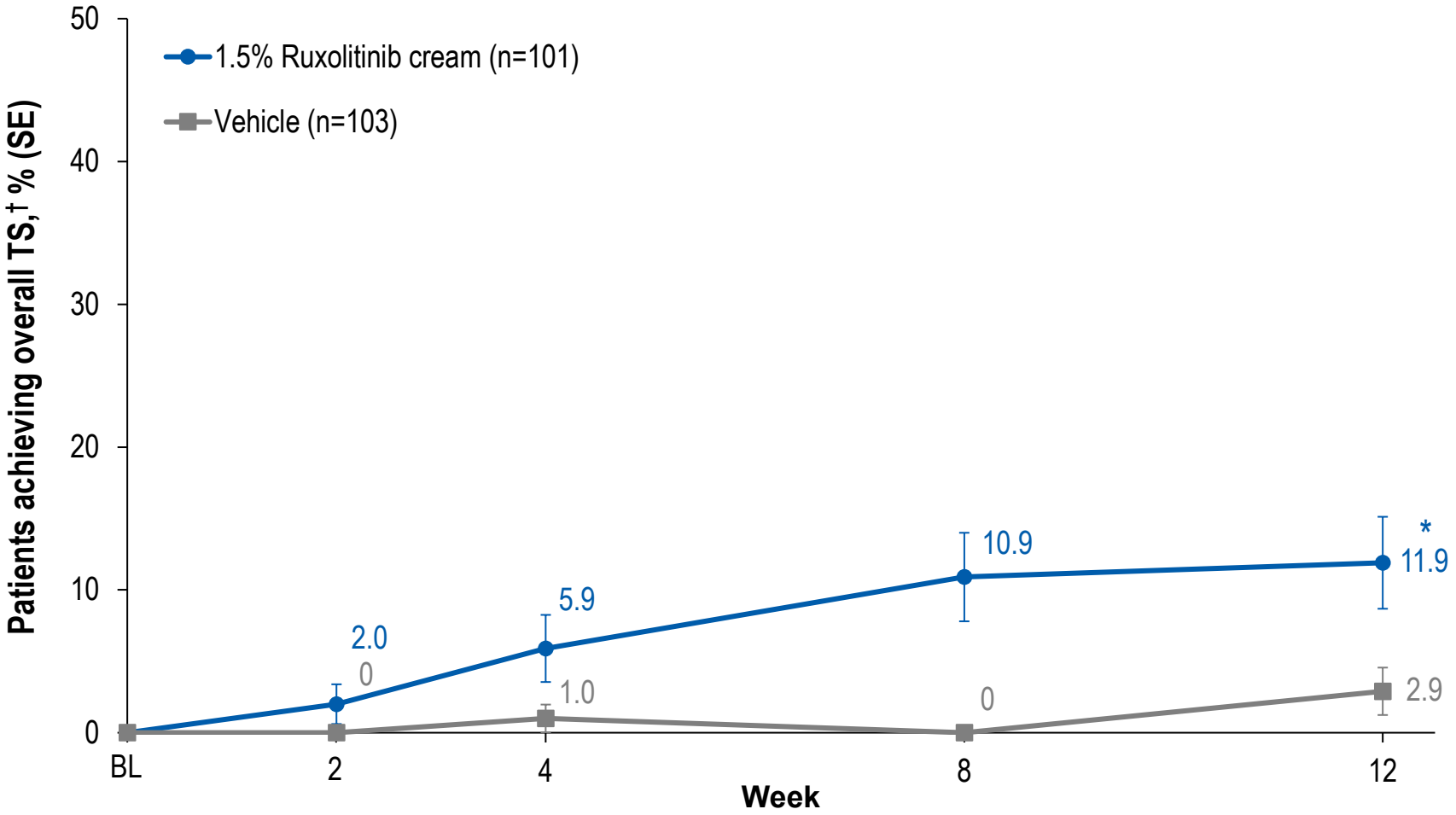
** *P*<0.01 vs vehicle.

P values were only assessed at Week 12 (Cochran-Mantel-Haenszel test stratified by baseline IGA-CPG-S score [2 or ≥3] and geographic region [North America or outside of North America]).

† IGA-CPG-S-TS was defined as an IGA-CPG-S score of 0 or 1 with a ≥2-grade improvement from baseline. Patients with missing data were imputed as nonresponders.

Overall TS (Achievement of WI-NRS4 and IGA-CPG-S-TS) by Visit

Nonresponder Imputation



* *P*<0.05 vs vehicle.

P values were only assessed at Week 12 (Cochran-Mantel-Haenszel test stratified by baseline IGA-CPG-S score [2 or ≥3] and geographic region [North America or outside of North America]).

† Patients with missing data were imputed as nonresponders.

Safety

Safety Summary

n (%)	Vehicle cream (n=103)	1.5% Ruxolitinib cream (n=100)†
Patients with TEAE	37 (35.9)	31 (31.0)
Patients with treatment-related TEAE	6 (5.8)	0
Patients with application site reaction	4 (3.9)	0
Patients with grade ≥3 TEAE‡	5 (4.9)	4 (4.0)
Patients with serious TEAE‡	5 (4.9)	3 (3.0)
Patients with TEAE leading to discontinuation of study drug	4 (3.9)	3 (3.0)

Most Common TEAEs§

n (%)	Vehicle cream (n=103)	1.5% Ruxolitinib cream (n=100)†
Nasopharyngitis	2 (1.9)	9 (9.0)
COVID-19	5 (4.9)	0
Headache	3 (2.9)	2 (2.0)
Application site pain	4 (3.9)	0
Diarrhea	2 (1.9)	2 (2.0)
Hypertension	2 (1.9)	1 (1.0)
Urinary tract infection	3 (2.9)	0
Fall	2 (1.9)	0
Gastroenteritis viral	0	2 (2.0)
Migraine	2 (1.9)	0
Pneumonia	2 (1.9)	0

TEAE, treatment-emergent adverse event.
† 1 patient randomized to 1.5% ruxolitinib cream did not apply study drug and was excluded from the safety analysis.
‡ None were considered related to treatment.
§ Occurred in ≥2 patients in either treatment group.

Results From TRuE-PN1 and TRuE-PN2

Endpoint, %	TRuE-PN1			TRuE-PN2 (Preliminary)		
	Vehicle (n=102)	1.5% Ruxolitinib cream (n=101)	2-Sided *P* value	Vehicle (n=96)	1.5% Ruxolitinib cream (n=93)	2-Sided *P* value[†]
WI-NRS4 at Week 12 (NRI) (Primary)	20.6	44.6	0.0003	36.2	40.0	0.59
WI-NRS4 at Week 4 (NRI)	12.7	29.7	0.0034	19.1	30.5	0.07
WI-NRS4 at Day 7 (MI)	8.0	22.4	0.0064	5.3	14.8	<0.05
IGA-CPG-S-TS at Week 12 (NRI)	3.9	15.8	0.0048	10.6	24.0	<0.05
Overall TS at Week 12 (NRI)	2.9	11.9	0.0164	6.4	12.5	0.15

- Baseline demographics and disease characteristics between TRuE-PN1 and TRuE-PN2 were similar
- The adverse event profile was also similar between the 2 studies
- Further analyses of both studies are ongoing

MI, multiple imputation; NRI, nonresponder imputation.
[†] For TRuE-PN2, *P* values are nominal for all secondary endpoints (WI-NRS4 at Week 4 and Day 7, IGA-CPG-S-TS at Week 12, overall TS at Week 12).

Pooled Analysis From TRuE-PN1 and TRuE-PN2

Endpoint, %	Vehicle (N=197)	1.5% Ruxolitinib cream (N=197)	Δ (*P* Value)†
WI-NRS4 at Week 12 (NRI)	28.1	42.3	14.4 (0.0029)
WI-NRS4 at Week 4 (NRI)	15.8	30.1	14.4 (0.0008)
WI-NRS4 at Day 7 (MI)	7.2	19.4	12.0 (0.0007)
IGA-CPG-S-TS at Week 12 (NRI)	7.1	19.8	12.6 (0.0002)
Overall TS at Week 12 (NRI)	4.6	12.2	7.6 (0.0066)

† Nominal *P* values were assessed using the Cochran-Mantel-Haenszel test stratified by baseline IGA-CPG-S score (2 or ≥3) and geographic region (North America or outside of North America).

Conclusions

- In the TRuE-PN1 study, 1.5% ruxolitinib cream BID demonstrated statistically significant improvement in the primary and all key secondary endpoints vs vehicle at Week 12
  - Significant itch improvements were seen at early study visits
  - Clinical improvements were also observed at the first assessment (Week 2)
- The overall safety profile of 1.5% ruxolitinib cream in the TRuE-PN clinical trial program was consistent with previous data, and no new safety signals were observed
- Ruxolitinib cream may be a novel approach for the treatment of PN

Thank You For Your Attention

The authors wish to thank the patients and their families, the investigators, and the site personnel who participated in this study

The authors would also like to acknowledge M. Celeste Ferreira-Cornwell, PhD, for her contributions to the study

To download Incyte content presented at AAD 2025, scan code.

For questions, please contact Shawn G. Kwatra (shawn.kwatra@gmail.com)

This study was sponsored by Incyte Corporation (Wilmington, DE).

Medical writing support was provided by Rob M. Camp, PhD, from The Curry Rockefeller Group, LLC, a Citrus Health Group, Inc., company (Chicago, IL), and was funded by Incyte Corporation.