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

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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.

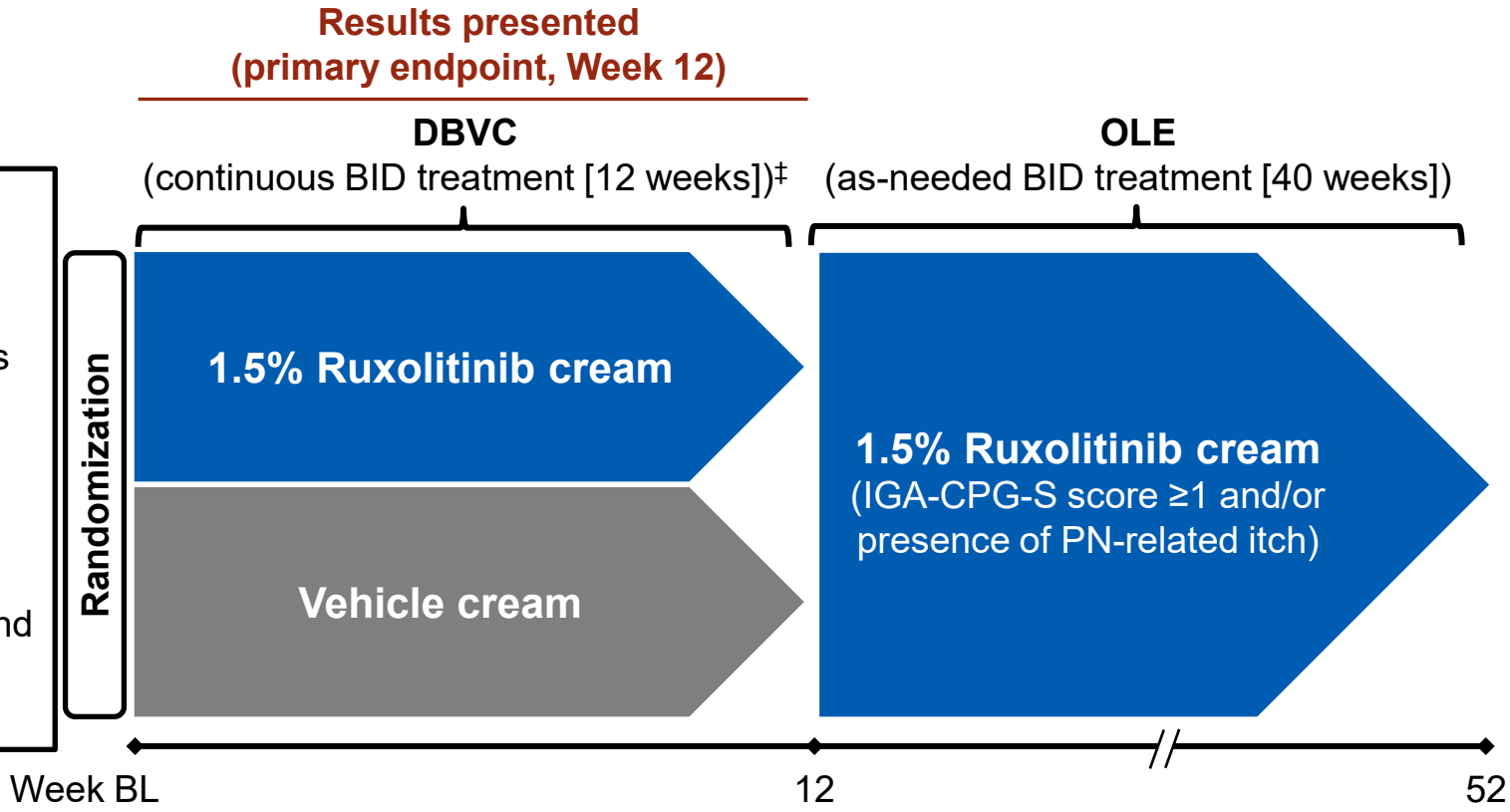
1. Elmariah S, et al. *J Am Acad Dermatol.* 2021;84(3):747-760. 2. Pereira MP, et al. *J Eur Acad Dermatol Venereol.* 2020;34(10):2373-2383. 3. Wong LS, Yen YT. *Int J Mol Sci.* 2022;23(20):12390. 4. Agrawal D, et al. *J Cosmet Dermatol.* 2022;21(9):4009-4015. 5. Fukushi S, et al. *Br J Dermatol.* 2011;165(5):990-996. 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)

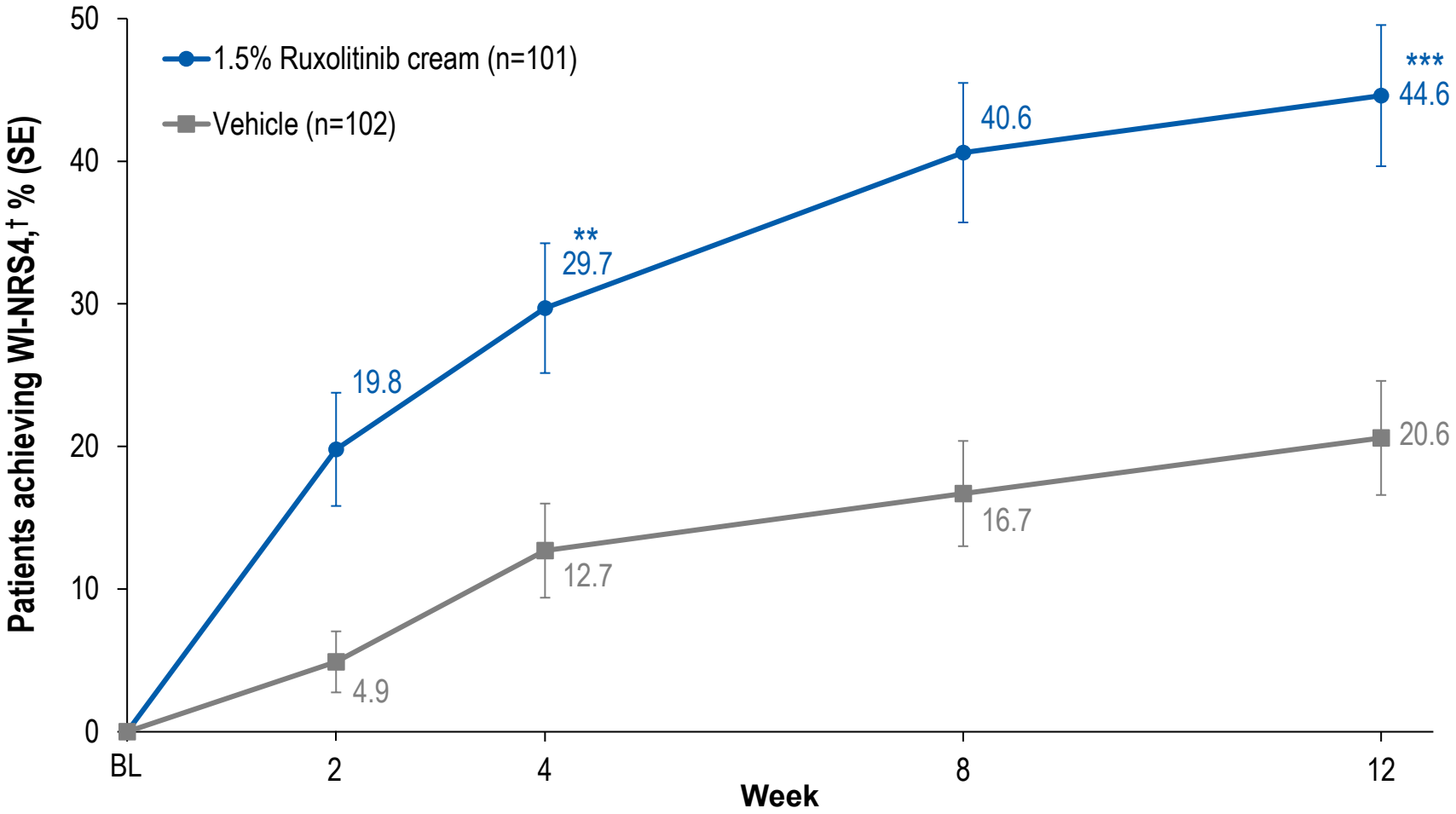
Clinical characteristics	Vehicle (n=103)	1.5% Ruxolitinib cream (n=101)
Disease duration, median (range), y	4.7 (0.3–45.4)	4.1 (0.3–66.8)
WI-NRS score, mean (SD)	8.4 (0.8)	8.4 (1.0)
Skin Pain NRS score, mean (SD)	7.5 (2.0)	7.1 (2.4)
Treatment BSA, mean (SD), %	8.8 (5.4)	8.8 (5.4)
IGA-CPG-S score, n (%)		
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



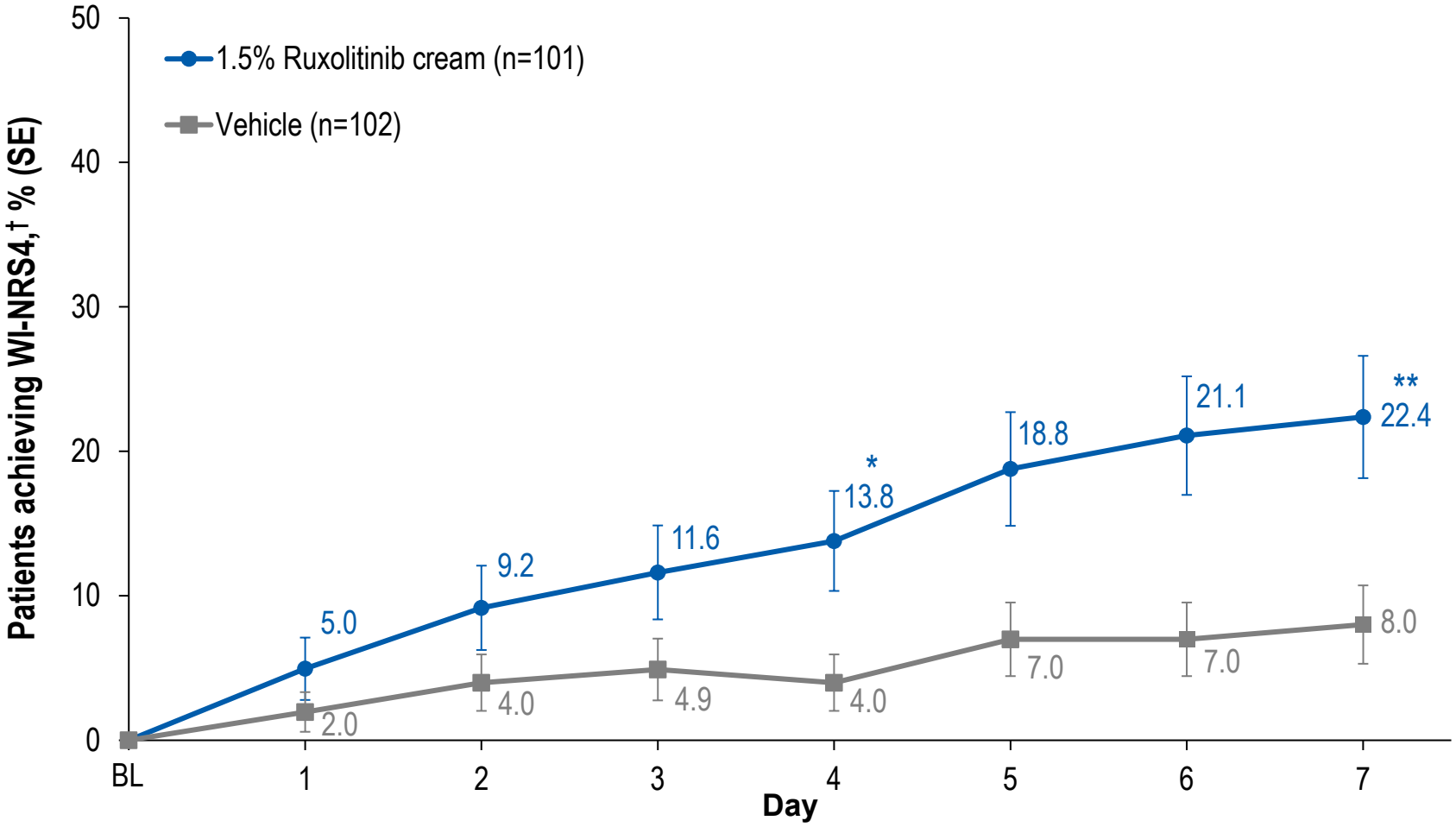
** *P*<0.01 vs vehicle; *** *P*<0.001 vs vehicle.

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

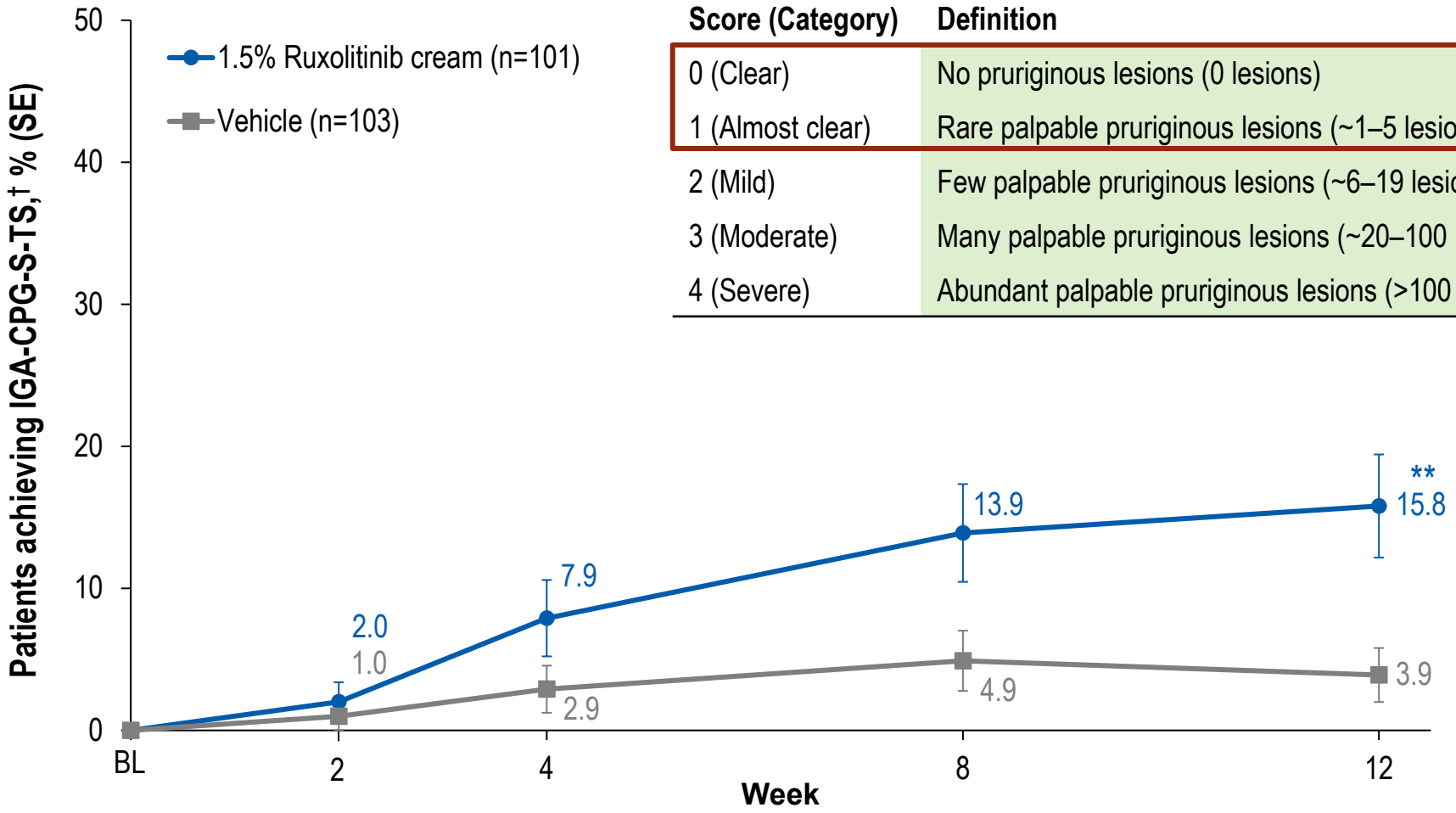
Multiple Imputation



* *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

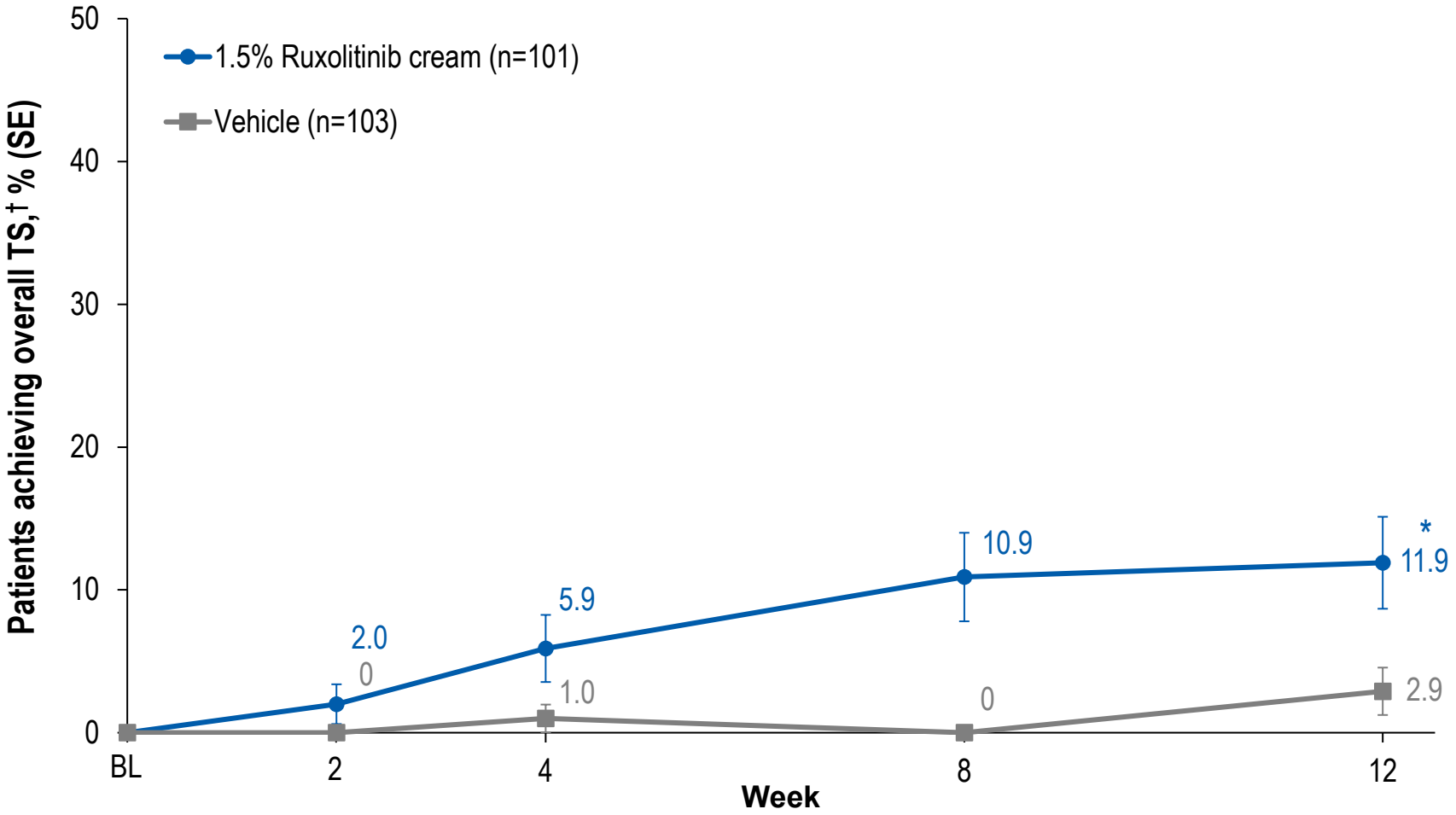
** *P*<0.01 vs vehicle.

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

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

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