Roflumilast Cream (ARQ-151) Improved Itch Severity and Itch-Related Sleep Loss in Adults With Chronic Plaque Psoriasis in a Phase 2b Study

Linda Stein Gold[1], Mark G. Lebwohl[2], Kim A. Papp[3], Melinda J. Gooderham[4], Leon H. Kircik[5], Zoe D. Draelos[6], Steven E. Kempers[7], David M. Pariser[8], Javier Alonso-Llamazares[9], Darryl P. Toth[10], Kathleen Smith[11], Robert C. Higham[11], Lynn Navale[11], Howard Welgus[11], David R. Berk[11]

[1]Henry Ford Medical Center, Detroit, MI, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [4]SkiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [5]Icahn School of Medicine at Mount Sinai, New York, NY; Indiana Medical Center, Indianapolis, IN; Physicians Skin Care, PLLC, Louisville, KY; and Skin Sciences, PLLC, Louisville, KY, USA; [6]Dermatology Consulting Services, High Point, NC, USA; [7]Minnesota Clinical Study Center, Fridley, MN, USA; [8]Department of Dermatology, Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; [9]Driven Research LLC, Coral Gables, FL, USA; [10]XLR8 Medical Research, Probity Medical Research, Windsor, ON, Canada; [11]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA.

Disclosures

L. Stein Gold is an investigator for AbbVie, Arcutis, Celgene, Dermavant, Eli Lilly, Leo, Novartis, and Ortho Derm; serves as an advisor for Celgene, Dermavant, Leo, Novartis, and Ortho Derm, and is a speaker for Leo and Ortho Derm.

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Background

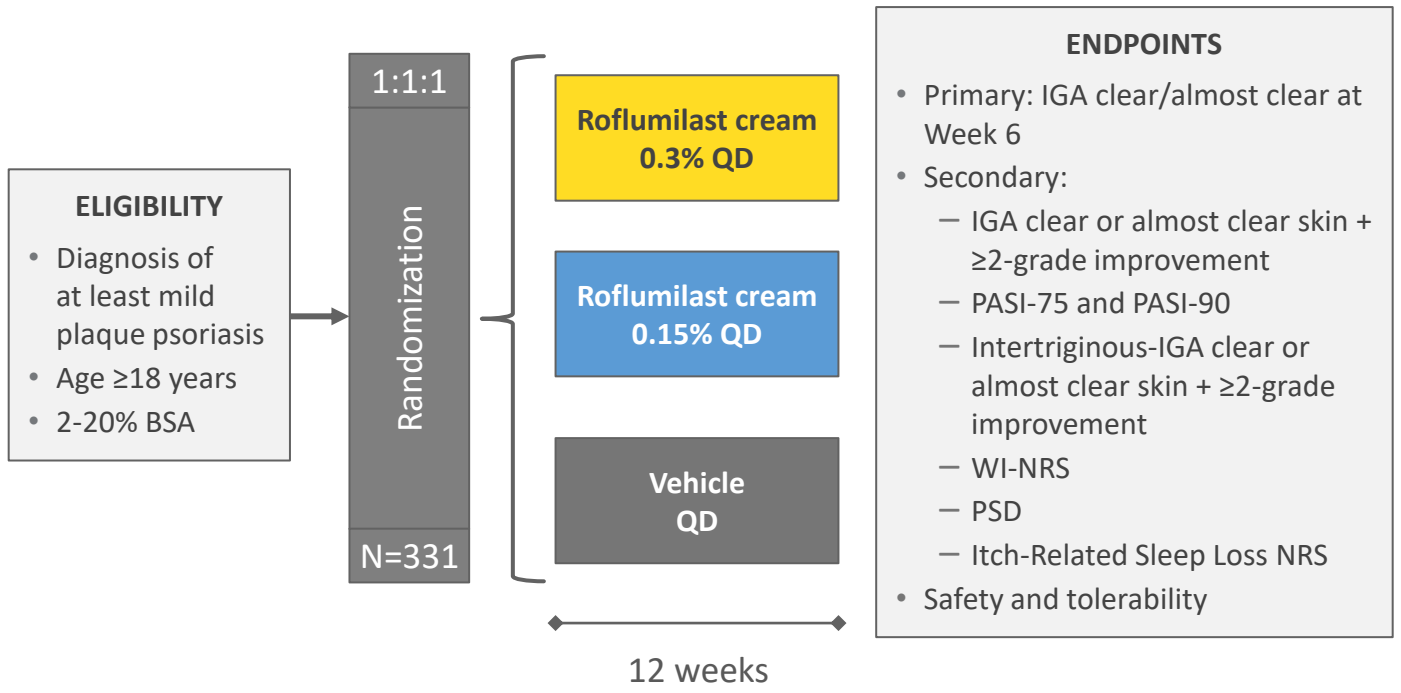
- Roflumilast cream (ARQ-151), a potent PDE-4 inhibitor, is under investigation as a once-daily topical treatment for plaque psoriasis[1,2]
- In a randomized, double-blind, phase 2b trial of 331 adults with chronic plaque psoriasis, roflumilast cream administered once daily was superior to vehicle cream[2]
  - Primary endpoint of achievement of clear or almost-clear skin based on IGA at Week 6 was met
    - Roflumilast 0.3% 28.0% (*P*<0.001 vs vehicle)
    - Roflumilast 0.15% 22.8% (*P*=0.004 vs vehicle)
    - Vehicle 8.3%
  - Treatment-related adverse events, including application site pain, were uncommon and the frequency was similar in all groups
- Here we report the effect of roflumilast cream on itch, a highly prevalent and frequently bothersome symptom of chronic plaque psoriasis that negatively impacts quality of life,[3] assessed using PRO measures in this study

IGA: Investigator Global Assessment; PDE-4: phosphodiesterase-4; PRO: patient-reported outcome.

[1]Papp KA, et al. *J Drugs Dermatol*. 2020;19:734-740. [2]Lebwohl MG, et al. *N Engl J Med*. 2020;383:229-239. [3]Naegeli AN, et al. *Int J Dermatol*. 2015;54:715-722.

Study Design

- Randomized, double-blind, vehicle-controlled multicenter study[1]
- **Itch** was assessed at baseline, Weeks 2, 4, 6, 8, and 12 using PRO measures:
  - **Worst Itch Numeric Rating Scale (WI-NRS)**[2] assessed the worst itch
  - **Psoriasis Symptom Diary (PSD) Items 1 and 2**[3-5] assessed burden and severity of itch
  - **Itch-Related Sleep Loss NRS** assessed intensity of sleep loss
  - All PRO measures assessed itch over the previous 24 hours and were rated on a scale from 0 (no impact) to 10 (as bad as it can be)



ClinicalTrials.gov NCT03638258. BSA: body surface area; IGA: Investigator Global Assessment; NRS: numeric rating scale; QD: once daily; PASI: Psoriasis Area and Severity Index; PRO: patient-reported outcome.

[1]Lebwohl MG, et al. *N Engl J Med*. 2020;383:229-239. [2]Naegeli AN, et al. *Int J Dermatol*. 2015;54:715-722. [3]Lebwohl M, et al. *Int J Dermatol*. 2014;53:714-722. [4]Strober BE, et al. *Value Health*. 2013;16:1014-1022. [5]Strober B, et al. *Int J Dermatol*. 2016;55:e147-e155.

Baseline Characteristics

	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=113)	Vehicle (n=109)
Age, mean (SD) years	51.7 (14.1)	54.4 (14.2)	55.5 (13.5)
Sex, male, n (%)	56 (51.4)	62 (54.9)	67 (61.5)
Race, n (%)			
White	82 (75.2)	95 (84.1)	92 (84.4)
Black	12 (11.0)	10 (8.8)	7 (6.4)
Multiple/other	15 (13.8)	8 (7.1)	10 (9.2)
Psoriasis-affected BSA, mean (SD), %	6.3 (4.0)	6.4 (3.9)	6.4 (3.6)
IGA score			
2 (mild), %	15.6	15.9	10.1
3 (moderate), %	77.1	73.5	81.7
4 (severe), %	7.3	10.6	8.3

	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=113)	Vehicle (n=109)
PASI, mean score (SD)	7.7 (3.6)	8.0 (3.9)	7.6 (3.1)
WI-NRS score ≥6, n (%)	71 (65.1)	62 (54.9)	64 (58.7)
WI-NRS, mean score* (SD)	6.1 (2.7)	5.6 (3.1)	5.9 (2.9)
PSD Item 1, Itch Severity,* mean score (SD)	5.5 (2.8)	5.3 (3.1)	5.5 (3.0)
PSD Item 2, Itch Burden,* mean score (SD)	5.2 (3.0)	5.2 (3.3)	5.5 (3.2)
Itch-related Sleep Loss NRS,* mean score (SD)	2.9 (3.2)	3.0 (3.2)	3.4 (3.2)

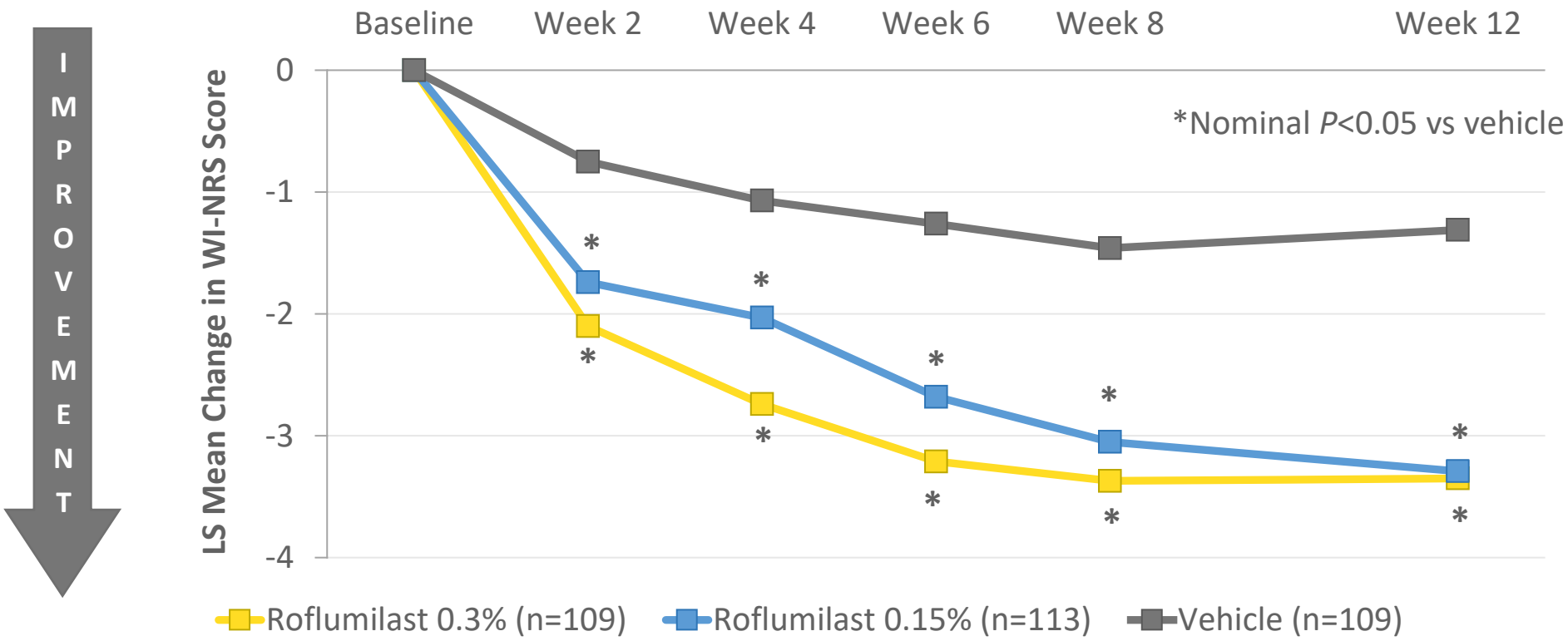
Data are presented for intent-to-treat population. *Scale of 0 (none) to 10 (worst). BSA: body surface area; IGA: Investigator Global Assessment; NRS: numeric rating scale PASI: Psoriasis Area and Severity Index; PSD: Psoriasis Symptom Diary; SD: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Lebwohl MG, et al. *N Engl J Med*. 2020;383:229-239.

Roflumilast Cream Significantly Reduced Patient-Reported Severity of Worst Itch

WI-NRS: "What was the worst level of itch over the past 24 hours?"

Assessed on a scale from 0 (no itch) to 10 (worst imaginable itch)



Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. LS: least squares; WI-NRS: Worst Itch Numeric Rating Scale.

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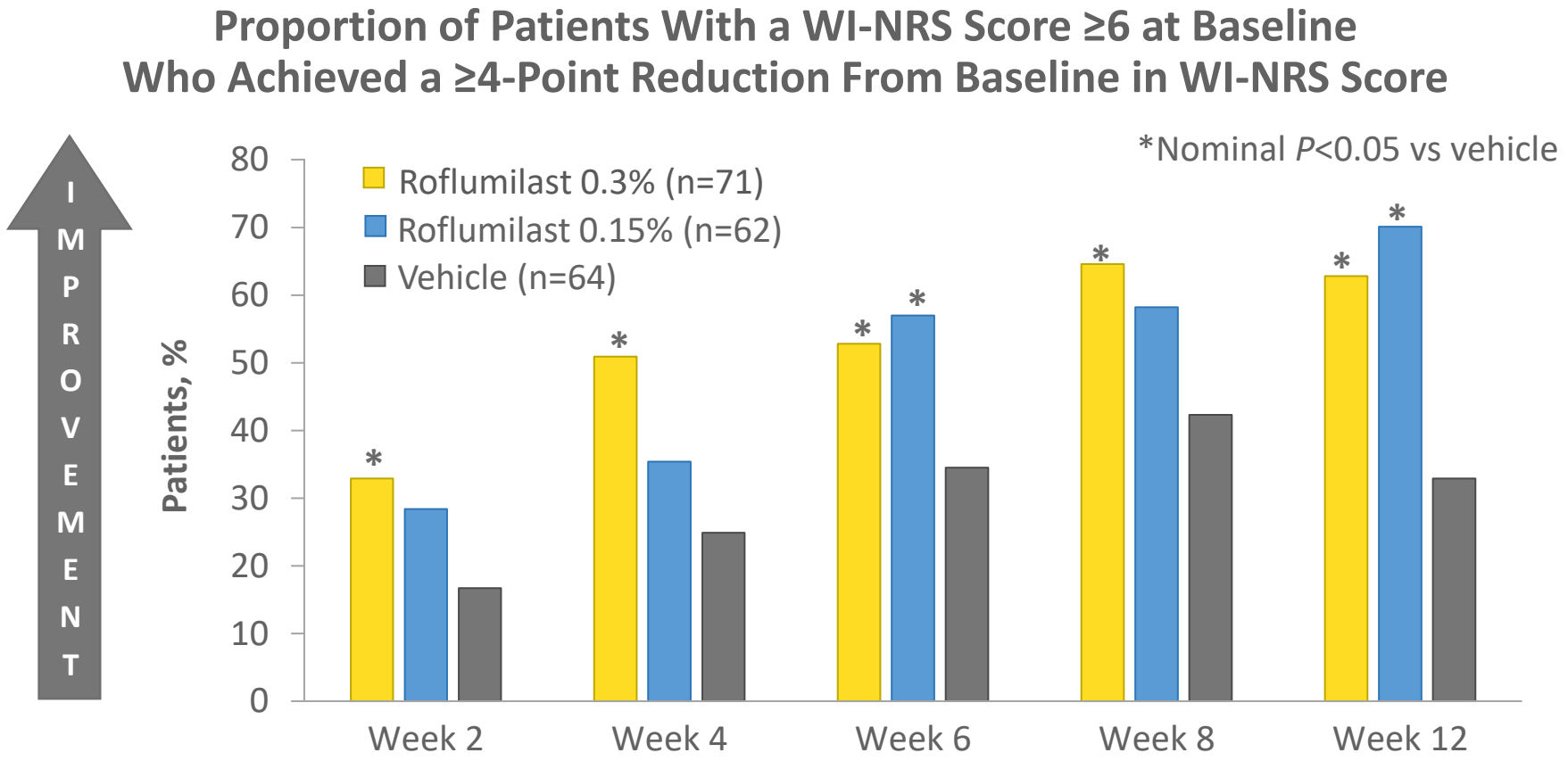
Roflumilast Cream Led to Significant Improvement in Itch Responder Rate

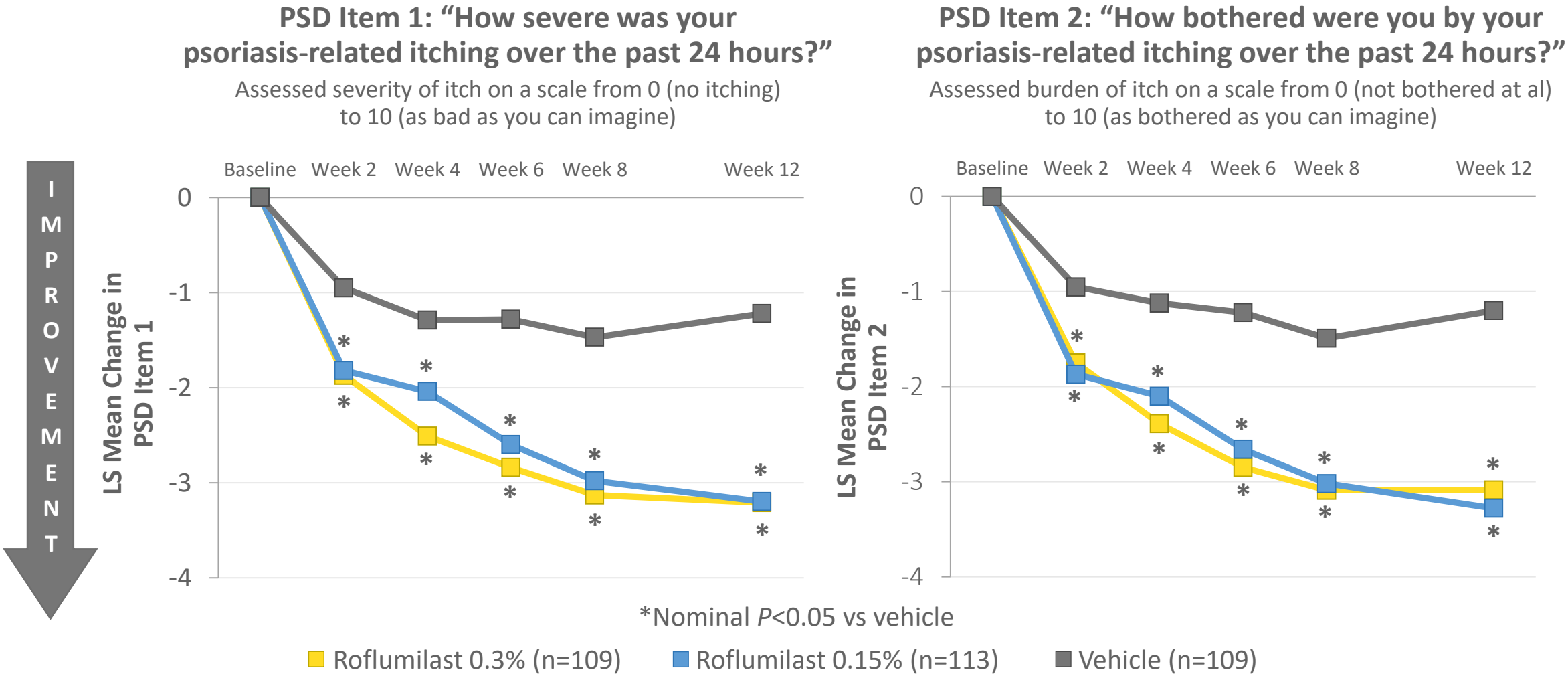


Previous studies have shown that a 4-point change is optimal for demonstrating a clinically meaningful itch response in patients with moderate-to-severe plaque psoriasis[1]

WI-NRS assessed the worst itch over the past 24 hours on a scale ranging from 0 (no itch) to 10 (worst imaginable itch). Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. WI-NRS: Worst Itch Numeric Rating Scale.

[1]Kimball AB, et al. *Br J Dermatol*. 2016;175:157-162.

Roflumilast Cream Significantly Reduced Patient-Reported Severity and Burden of Itch



Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. LS: least squares; PSD: Psoriasis Symptom Diary.

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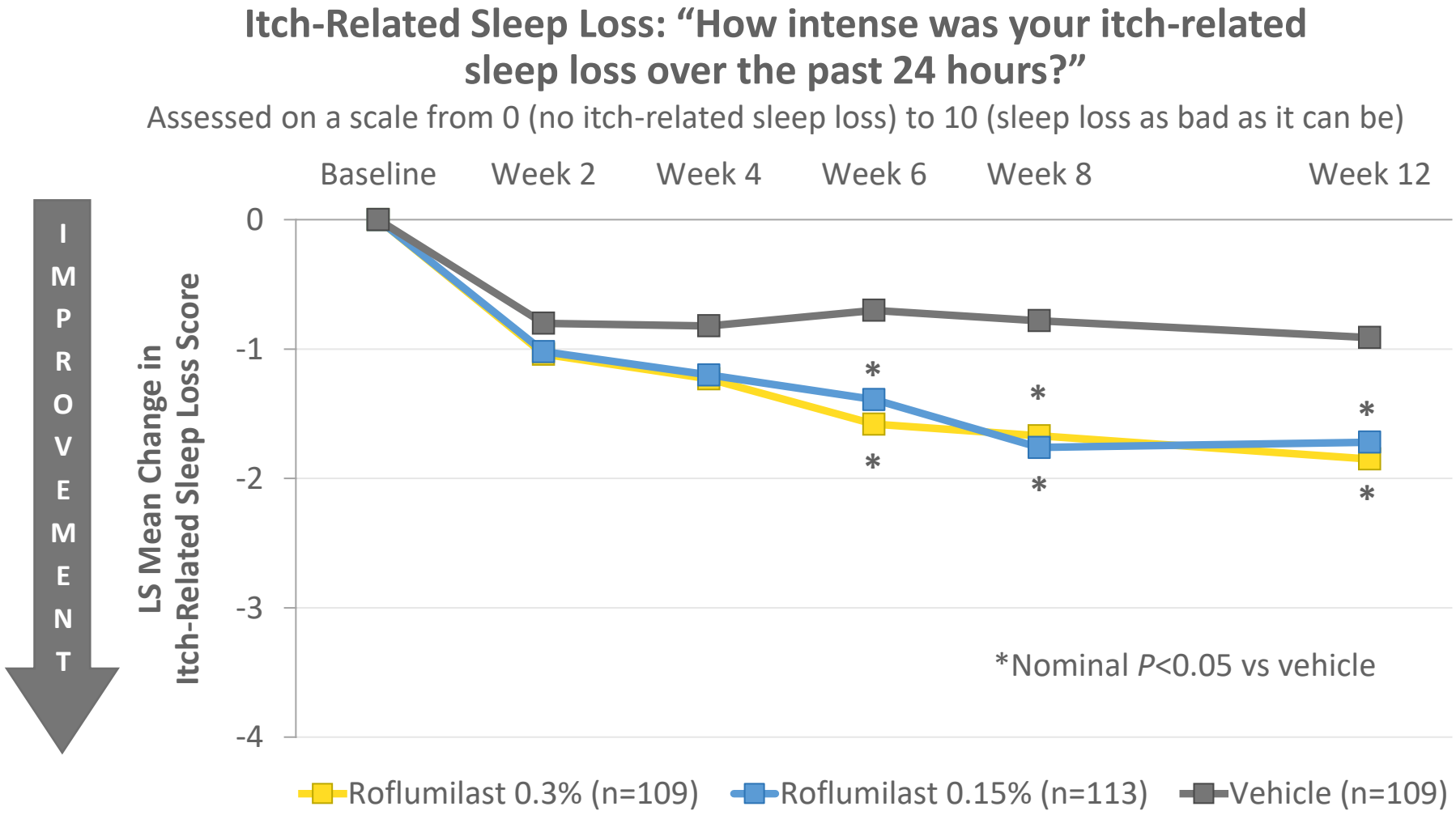
Roflumilast Cream Significantly Reduced Patient-Reported Sleep Loss Related to Itch



Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. LS: least squares; NRS: numeric rating scale.

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TEAEs Were Uncommon

- More patients discontinued the study due to an AE in the vehicle group than in the roflumilast groups
- Rates of application site pain were low and similar to vehicle
- 97% of AEs were rated mild or moderate

TEAE, n (%)	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=110)	Vehicle (n=107)
Patients with any TEAE	42 (38.5)	30 (27.3)	32 (29.9)
Patients with any treatment-related TEAE	7 (6.4)	3 (2.7)	7 (6.5)
Patients with any SAE[a]	1 (0.9)	1 (0.9)	2 (1.9)
Patients who discontinued study due to AE[b]	1 (0.9)	0	2 (1.9)
Most common TEAE (>2% patients in any group)			
Upper respiratory tract infection (including viral)	9 (8.3)	8 (7.3)	4 (3.7)
Nasopharyngitis	4 (3.7)	3 (2.7)	4 (3.7)
Application site pain	2 (1.8)	1 (0.9)	3 (2.8)
Sinusitis	3 (2.8)	0	0
Urinary tract infection	0	3 (2.7)	1 (0.9)

[a]Roflumilast 0.3%: worsening of chest pain in a patient with history of myocardial infarction; roflumilast 0.15%: melanoma (not in treatment area); vehicle group: acute infarction of left basal ganglia, spontaneous miscarriage. [b]Roflumilast 0.3%: onset of worsening psoriasis; vehicle: mood swings, contact dermatitis.

Data are presented for safety population. AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Lebwohl MG, et al. *N Engl J Med*. 2020;383:229-239.

Conclusions

- Once-daily roflumilast cream demonstrated significant improvement in reducing itch in patients with psoriasis compared with vehicle cream
  - Patients reported a rapid and clinically significant reduction in the severity and burden of itch
  - Significant itch reduction occurred by Week 2 and continued with further reductions through Week 12
  - In a subgroup of patients with greater severity of itch at baseline (WI-NRS ≥6), more than half of the patients had a substantial (≥4-point) reduction in itch by Week 6, and the response rate continued to increase through Week 12
  - Reduction in itch resulted in significant improvement in sleep loss by Week 6
- Roflumilast cream was well-tolerated and application site pain was uncommon and similar to vehicle

In a Phase 2b study, **roflumilast cream**, an investigational once-daily, non-steroidal topical PDE-4 inhibitor, was effective in achieving clear or almost clear skin and improving itch and itch-related sleep loss in patients with chronic plaque psoriasis

PDE-4: phosphodiesterase-4; WI-NRS: Worst Itch Numeric Rating Scale.

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