Once-daily Roflumilast Foam 0.3% for Scalp and Body Psoriasis: A Randomized, Double-blind, Vehicle-controlled Phase 2b Study

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Disclosures

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Introduction

- In patients with psoriasis, about 80% have scalp psoriasis (S-PsO)[1]
  - S-PsO is often associated with itch, the most burdensome symptom of psoriasis[2]
  - Itching, flaking, and appearance of plaques on the scalp can cause social embarrassment and adversely impact quality of life[3]
  - Treatment of S-PsO is difficult because the hair may limit efficacy of creams and ointments and reduce treatment adherence[4]
- Roflumilast is a potent, nonsteroidal, phosphodiesterase-4 inhibitor being investigated as a topical treatment for various dermatologic conditions
  - Roflumilast cream met the primary and secondary endpoints and was well-tolerated in a phase 2b randomized, double-blind, vehicle-controlled trial in adults with psoriasis[5]
- We investigated roflumilast foam for S-PsO and body PsO in a phase 2b randomized, double-blind, vehicle-controlled 8-week study

1. Chan CS, et al. J Am Acad Dermatol 2009;60:962-71.; 2. Elewski B, et al. J Eur Acad Dermatol Venereol. 2019;33:1465-1476. 3. Dopytalska K et al. Reumatologia. 2018;56:392-8. 4. Blakely K, Gooderham M. Psoriasis (Auckl). 2016;6:33-40; 5. Lebwohl MG, et al. NEJM 2020;383:229-39

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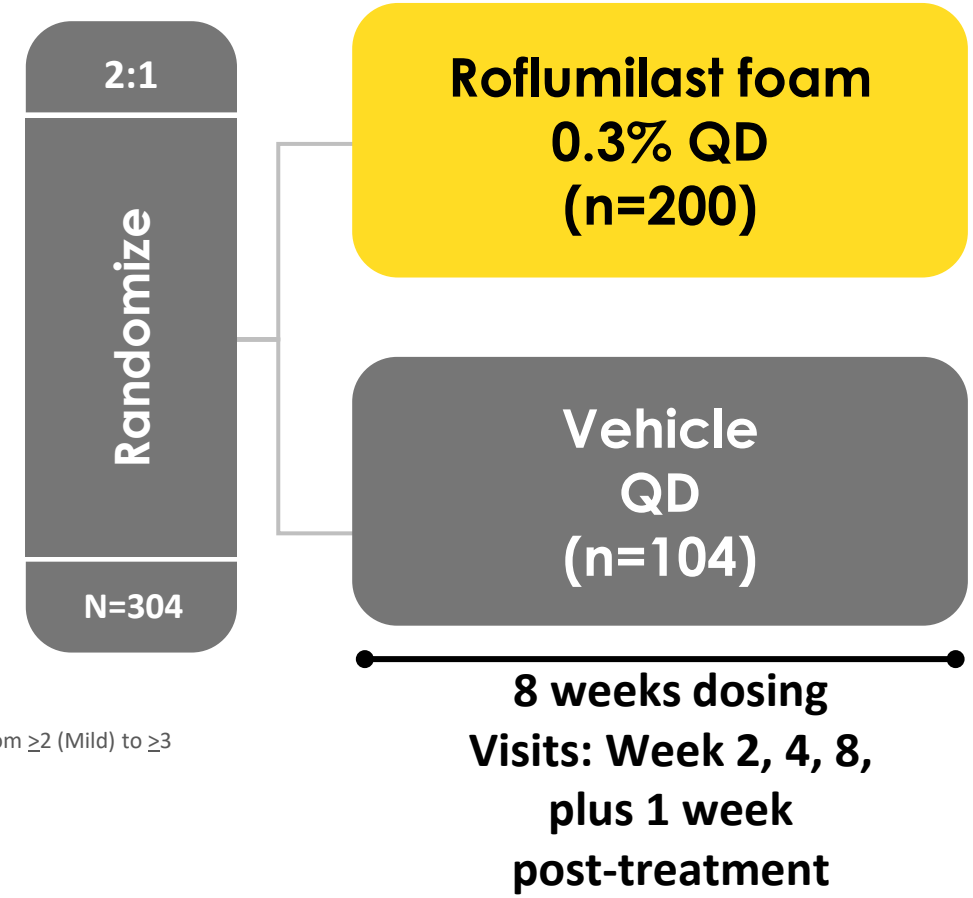
Methods and Study Design

Eligibility

- Aged ≥12y
- Diagnosis of scalp and body plaque psoriasis
- At least Mild severity* on both scalp (S-IGA) and body (B-IGA) IGAs
- ≤25% BSA
- Psoriasis Scalp Severity Index (PSSI) ≥6
- ≥10% of scalp involved
- Psoriasis Area Severity Index (PASI) ≥2



Endpoints

Primary

Scalp-IGA (S-IGA) success (Clear or Almost Clear with at least a 2-grade improvement from baseline)

Secondary

Body-IGA (B-IGA) success

Scalp worst itch NRS (SI-NRS)

Psoriasis Scalp Severity Index (PSSI-75)

Safety and Tolerability

*Protocol Amendment 2: S-IGA entry criterion changed from ≥2 (Mild) to ≥3 (Moderate)

- 96% power at α=0.05 to detect 22.4% difference between groups for S-IGA success, based on 201 results showing 32.2% vs. 9.8% IGA Success at Week 8[1]

BSA: body surface area; IGA: Investigator's Global Assessment; NRS: numeric rating scale; QD: once daily

1. Lebwohl MG, et al. NEJM 2020;383:229-39

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Subject Disposition

	Roflumilast foam 0.3% (N=200)	Vehicle foam (N=104)	Overall (N=304)
Completed	177 (88.5%)	87 (83.7%)	264 (86.8%)
Prematurely discontinued	23 (11.5%)	17 (16.3%)	40 (13.2%)
Reason for discontinuation			
Withdrawal by subject	9 (4.5%)	6 (5.8%)	15 (4.9%)
Non-compliance	1 (0.5%)	0	1 (0.3%)
Protocol violation	0	0	0
Lost to follow-up	8 (4.0%)	7 (6.7%)	15 (4.9%)
Adverse event	5 (2.5%)	2 (1.9%)	7 (2.3%)
Other	0	2 (1.9%)	2 (0.7%)

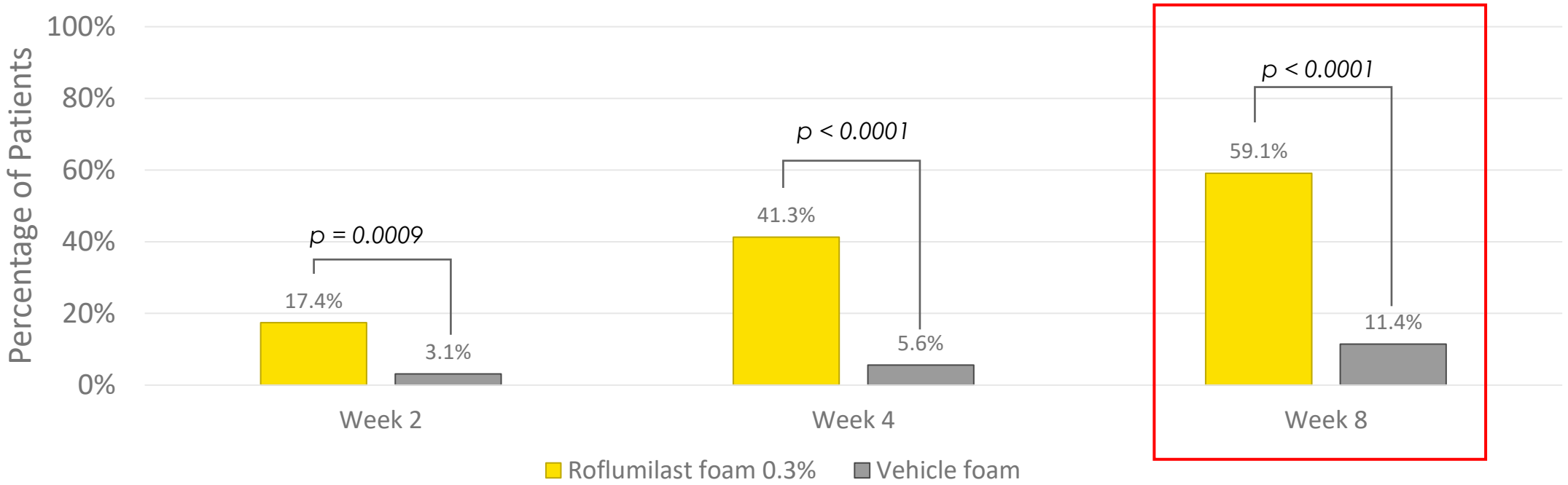
Baseline Disease Characteristics (ITT Population)

	Roflumilast foam 0.3% (N=200)†	Vehicle foam (N=104)	Overall (N=304)
BSA, mean %	8.0	7.6	7.9
Baseline S-IGA			
2 – Mild	18 (9.0%)	14 (13.5%)	32 (10.5%)
3 – Moderate	151 (75.5%)	80 (76.9%)	231 (76.0%)
4 – Severe	29 (14.5%)	10 (9.6%)	39 (12.8%)
Baseline B-IGA			
2 – Mild	69 (34.5%)	39 (37.5%)	108 (35.5%)
3 – Moderate	119 (59.5%)	60 (57.7%)	179 (58.9%)
4 – Severe	10 (5.0%)	5 (4.8%)	15 (4.9%)
PSSI, mean (SD)	22.4 (12.5)	20.9 (11.7)	21.9 (12.3)
PASI, mean (SD)	7.2 (4.3)	6.8 (4.4)	7.0 (4.3)
SI-NRS, mean (SD)	6.4 (2.4)	6.6 (2.3)	6.5 (2.3)
SI-NRS, ≥4, N (%)	173 (86.5%)	96 (92.3%)	269 (88.5%)

†Two patients were missing baseline values due to capture outside of the date-time visit window and were not evaluable.

Roflumilast Foam Significantly Increased the Percentage of Patients with S-IGA Success at Week 8 (Primary Endpoint)

Approx 60% of Patients Achieved S-IGA Success at Week 8
Significant Efficacy was Demonstrated as Early as Week 2



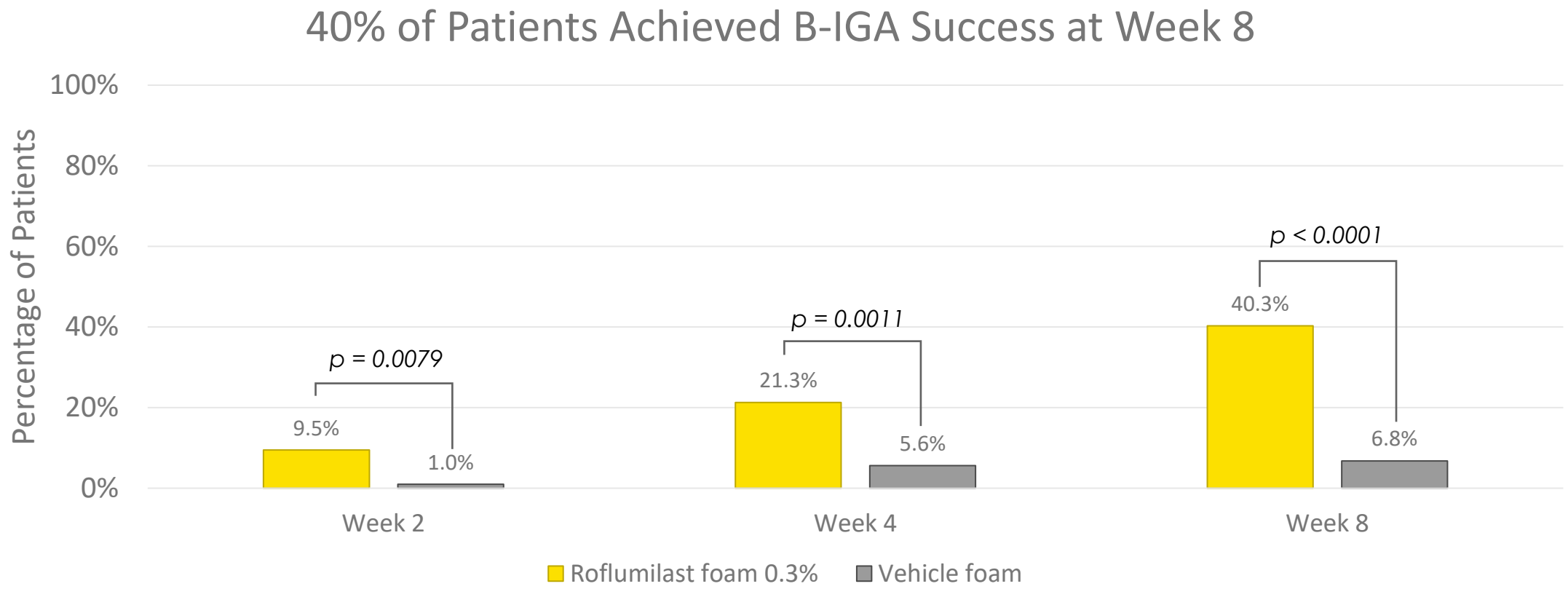
34.3% of patients on roflumilast achieved S-IGA = 0 (clear) versus 3.4% on vehicle

IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline

Intent-to-treat population

S-IGA: Scalp-Investigator's Global Assessment

Significantly More Patients Treated with Roflumilast Foam Had B-IGA Success as Early as Week 2



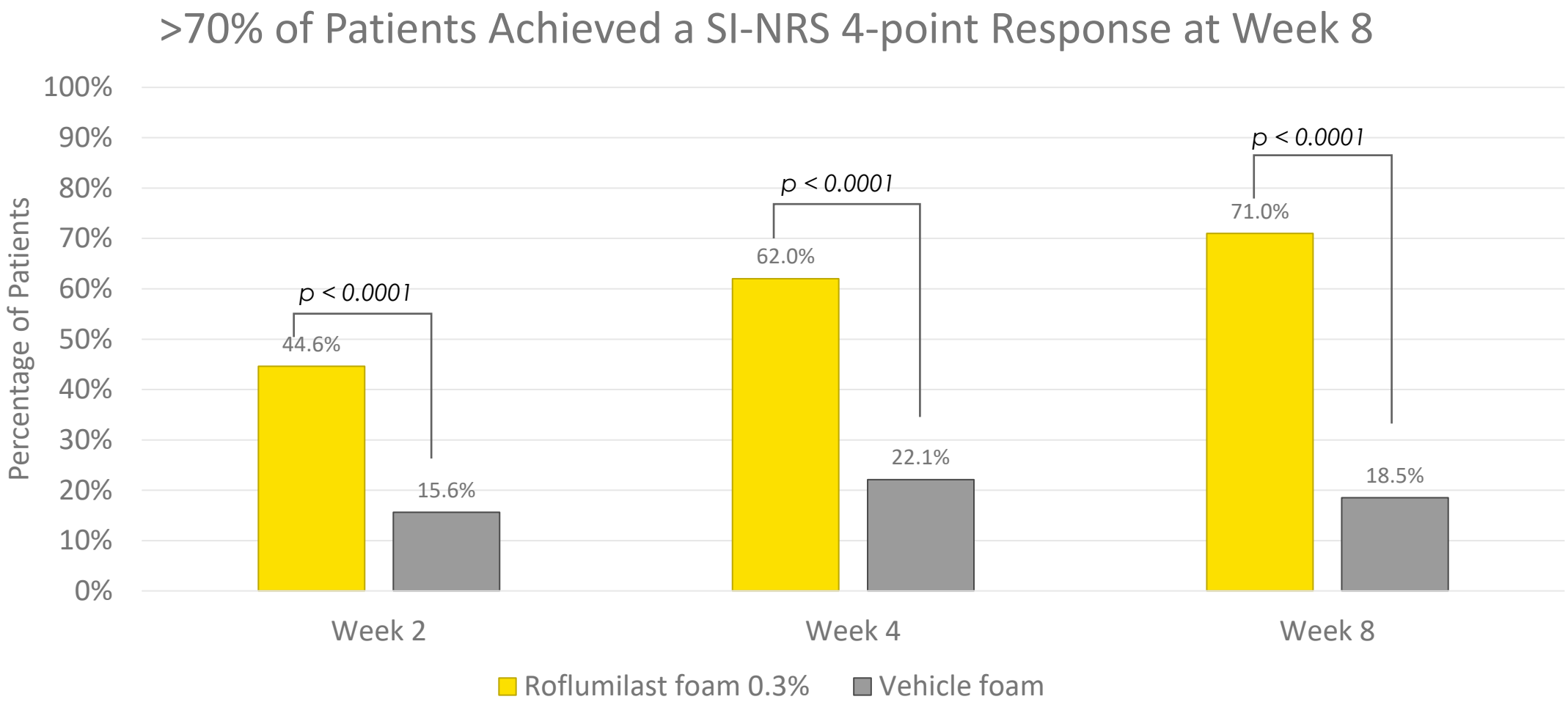
26.0% of patients on active achieved B-IGA = 0 (clear) versus 3.4% on vehicle

IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline

B-IGA: Body-Investigator's Global Assessment

Intent-to-treat population

Significantly More Roflumilast-treated Patients had SI-NRS 4-point Response as Early as Week 2



Evaluated in patients with SI-NRS Score ≥4 at Baseline

SI-NRS: Scalp worst itch numeric rating scale

Intent-to-treat population

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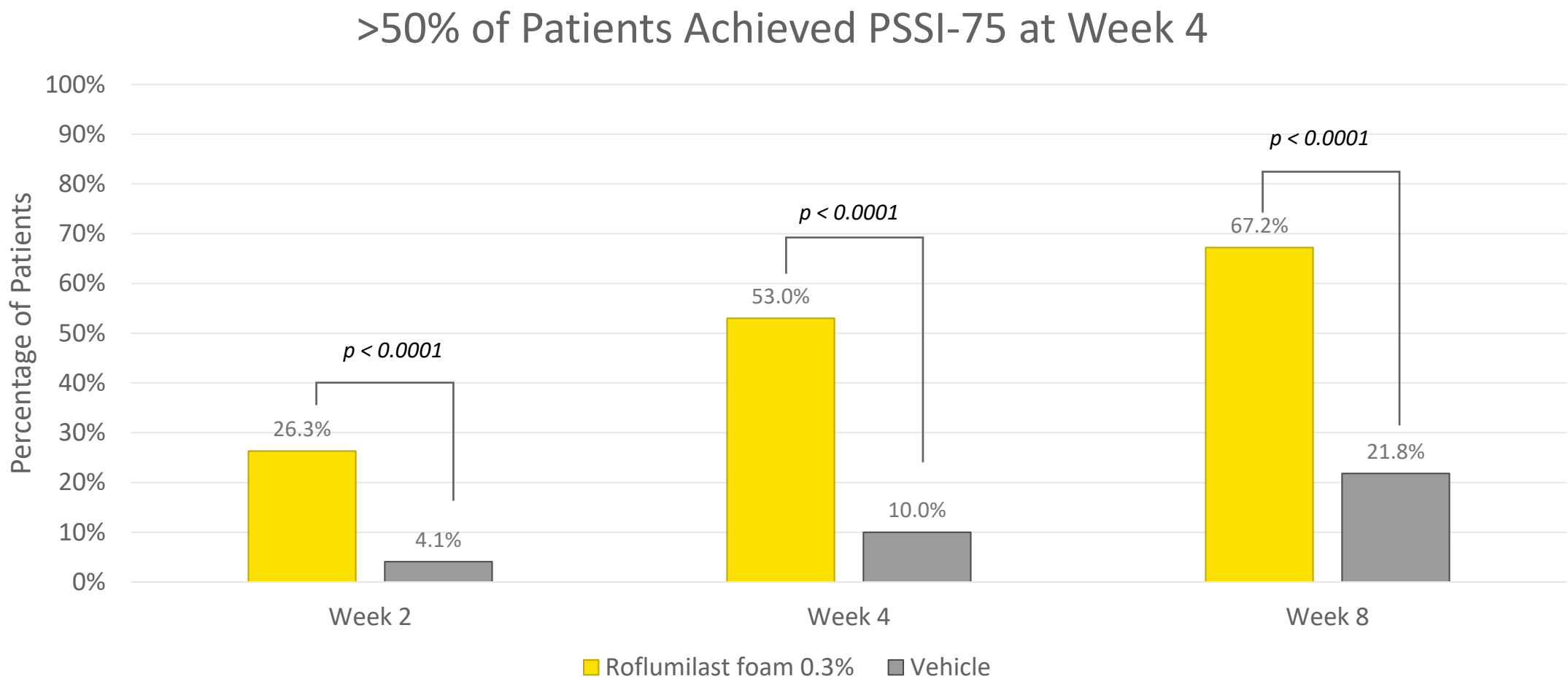
Significantly more Roflumilast-treated Patients Achieved a 75% Reduction in the Psoriasis Scalp Severity Index (PSSI-75)



IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline

Intent-to-treat population

Roflumilast Foam Had Safety and Tolerability Profile Similar to Vehicle

- Rates of AEs were low
- Few treatment-related AEs were reported
- Only 1 patient had a SAE (unrelated)
- Very few AEs lead to study discontinuation
  - Discontinuation rates were similar between groups
- ≥99% of roflumilast- and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator-rating of local tolerability

N (%)	Roflumilast foam 0.3% (n=198)	Vehicle foam (n=104)
Patients with any TEAE	46 (23.2)	20 (19.2)
Patients with any treatment-related TEAE	8 (4.0)	9 (8.7)
Patients with any SAE[a]	1 (0.5)	0 (0.0)
Patients who discontinued study due to AE[b]	5 (2.5)	2 (1.9)
Most common TEAE (>1.5% in any group), preferred term		
Application site pain	2 (1.0)	4 (3.8)
COVID-19	3 (1.5)	2 (1.9)
Psoriasis	1 (0.5)	2 (1.9)
Sinusitis	1 (0.5)	2 (1.9)
Hypertension	3 (1.5)	1 (1.0)
Diarrhea	3 (1.5)	0 (0.0)

[a]SAE = Testicular torsion, unrelated
[b]AE leading to discontinuation: roflumilast: application site pruritus, abdominal discomfort, diarrhea, headache, application site pain, application site discoloration, application site irritation, lethargy. vehicle arm: psoriasis, application site dermatitis.

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

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Conclusions

- Patients with scalp psoriasis need topical treatments that provide effective control of psoriasis with low incidence of side effects
- In this Phase 2b study, once-daily roflumilast foam significantly improved both scalp and body psoriasis, apparent as early as 2 weeks after treatment initiation
  - Roflumilast foam provided a robust and rapid reduction in itch that was maintained throughout the study
- Roflumilast foam was well-tolerated with low rates of TEAEs, application site AEs, and discontinuations due to AE
  - Rates of these events were similar to vehicle.
- Once-daily roflumilast foam is a potentially new novel therapy for the treatment of scalp and body psoriasis

AE: adverse event; TEAE: treatment-emergent adverse event.

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