Roflumilast Foam 0.3% in Patients With Scalp and Body Psoriasis in the Phase 3 ARRECTOR Trial: Efficacy, Patient-Reported Outcomes, and Safety

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Introduction

- Plaque psoriasis is a chronic inflammatory skin condition that negatively impacts quality of life[1]
  - Disease severity scores may underestimate the impact of disease severity on overall quality of life[1]
  - Up to 80% of patients with psoriasis experience scalp psoriasis[2-4]
- Roflumilast is a potent phosphodiesterase-4 (PDE4) inhibitor being investigated as a once-daily, nonsteroidal cream and foam formulation for long-term management of various dermatologic conditions:
  - Chronic plaque psoriasis (0.3% cream)
    - Approved for patients ≥12 years of age (US FDA and Health Canada)
  - Atopic dermatitis (0.05% and 0.15% cream)
  - Seborrheic dermatitis (0.3% foam)
- Roflumilast foam 0.3% differs from other topical foams:
  - Adapted from the high water-content formulation of roflumilast cream 0.3%
  - Excipients include an emulsifier novel to prescription topical products, which does not extract epidermal lipids at safe skin temperatures[5]
  - Does not contain ethanol, propylene glycol, or fragrances that can irritate skin

1. Golbari NM, et al. J Eur Acad Dermatol Venereol. 2021;35:417-421. 2. Callis Duffin K, et al. Dermatology 2021;237:46-55. 3. Egeberg A, et al. BMC Dermatol 2020;20:3. 4. van de Kerkhof PC, et al. Dermatology 1998;197:31-36. 5. Berk D, Osborne DW. Poster presented at the Society for Investigative Dermatology Annual Meeting, May 18–22, 2022, Portland, OR, USA.

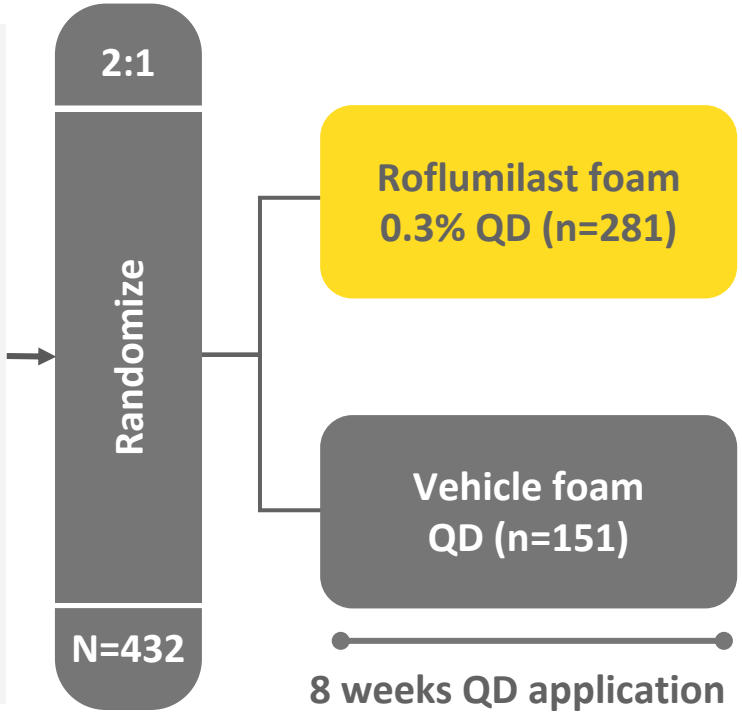
Phase 3 Trial of Roflumilast Foam 0.3% in Patients With Scalp and Body Psoriasis

Randomized, Parallel group, Double-blind, Vehicle-controlled, Multicenter Study

Objective: Assess the safety and efficacy of roflumilast foam 0.3% versus vehicle foam administered once-daily for 8 weeks in adolescent and adult patients with scalp and body psoriasis

Eligibility

- Aged ≥12 years
- Diagnosis of scalp and body plaque psoriasis
- At least Moderate severity on scalp (S-IGA) and Mild severity for body (B-IGA)
- ≤25% BSA
  - ≤20% non-scalp BSA
  - ≥10% of scalp involved
- PSSI ≥6
- PASI ≥2



Endpoints

Co-Primary

- S-IGA Success at Week 8
- B-IGA Success at Week 8

Secondary

- SI-NRS
- WI-NRS
- PASI-75
- PSD
- PSSI-75
- S-IGA=0

Safety and Tolerability

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

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

B-IGA: Body-Investigator Global Assessment; BSA: body surface area; PSD: psoriasis symptom diary; PASI: Psoriasis Area and Severity Index; PASI-75: 75% reduction in PASI; PSSI: Psoriasis Scalp Severity Index; PSSI-75, 75% reduction in PSSI; QD: once daily; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Baseline Demographics

Patients, n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle Foam (n=151)
Age, years, mean (SD)	**48.6 (14.9)**	**45.0 (14.3)**
Gender		
Male	129 (45.9)	60 (39.7)
Female	152 (54.1)	91 (60.3)
Ethnicity		
Hispanic or Latino	48 (17.1)	28 (18.5)
Not Hispanic or Latino	224 (79.7)	121 (80.1)
Not reported	9 (3.2)	2 (1.3)
Race		
American-Indian or Alaskan Native	0	3 (2.0)
Asian	26 (9.3)	4 (2.6)
Black or African American	12 (4.3)	6 (4.0)
Native Hawaiian, Other Pacific Islander	3 (1.1)	1 (0.7)
White	225 (80.1)	129 (85.4)
Other	11 (3.9)	7 (4.6)
More than one race	4 (1.4)	1 (0.7)

Baseline Disease Characteristics

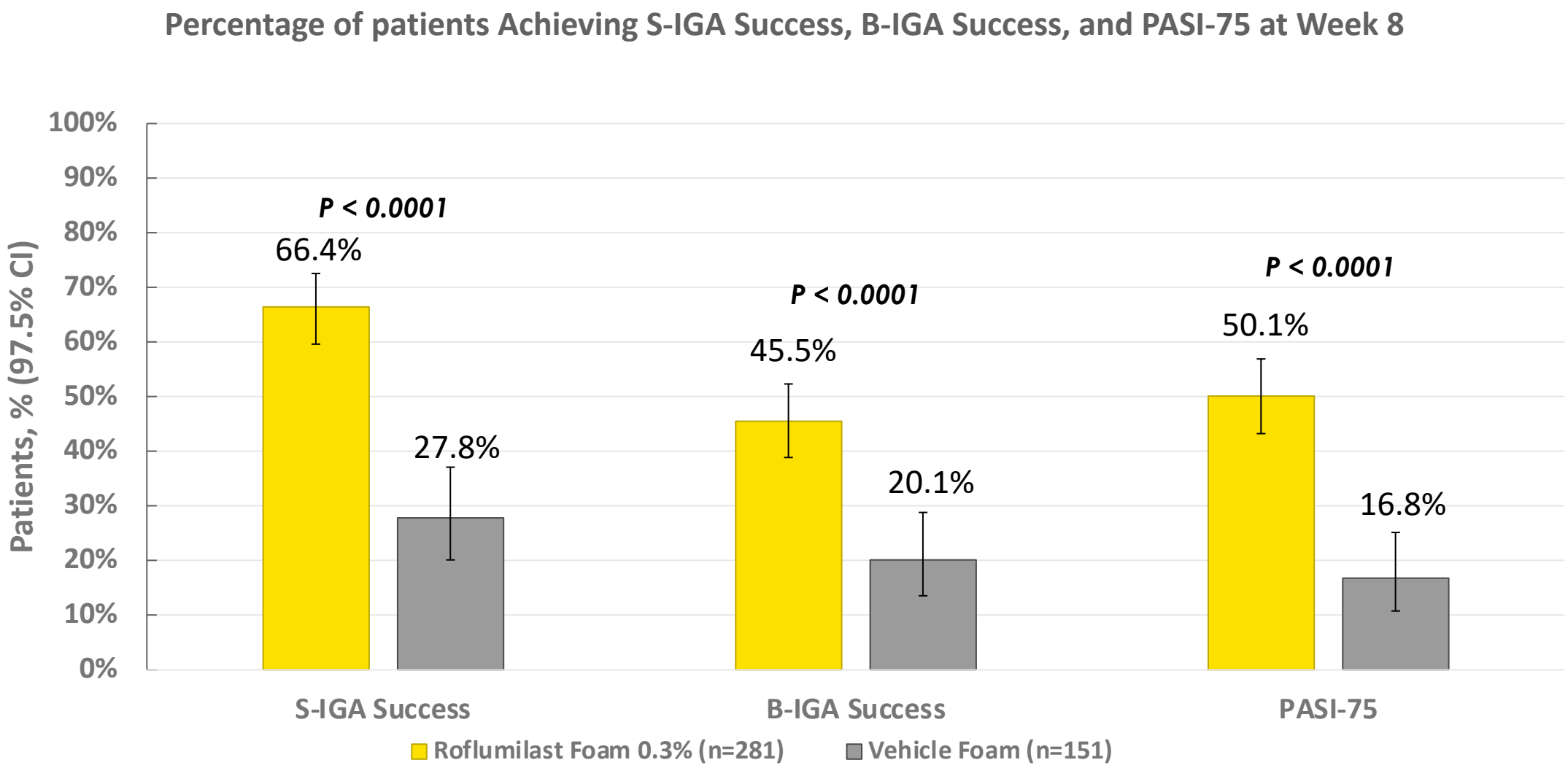
Patients, n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle (n=151)
BSA (%), mean (SD)	6.1 (4.3)	6.0 (4.3)
Extent of Scalp Involvement (%), mean (SD)	34.4 (25.0)	36.0 (25.8)
Baseline S-IGA		
3 (moderate)	239 (85.1)	131 (86.8)
4 (severe)	42 (14.9)	20 (13.2)
Baseline B-IGA		
2 (mild)	76 (27.0)	43 (28.5)
3 (moderate)	191 (68.0)	99 (65.6)
4 (severe)	14 (5.0)	9 (6.0)
PASI, mean (SD)	6.7 (3.6)	6.0 (3.3)
PSD, total mean (SD)	73.4 (40.2)	75.2 (36.9)
SI-NRS, mean (SD)	5.8 (2.6)	6.1 (2.3)
WI-NRS, mean (SD)	5.7 (2.6)	5.5 (2.6)

B-IGA: Body-Investigator Global Assessment; BSA: body surface area; PASI: Psoriasis Area and Severity Index; PSD: Psoriasis Symptom Diary; PSSI: Psoriasis Scalp Severity Index; SD: standard deviation; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale

Previous Treatment History of Scalp and Body Psoriasis

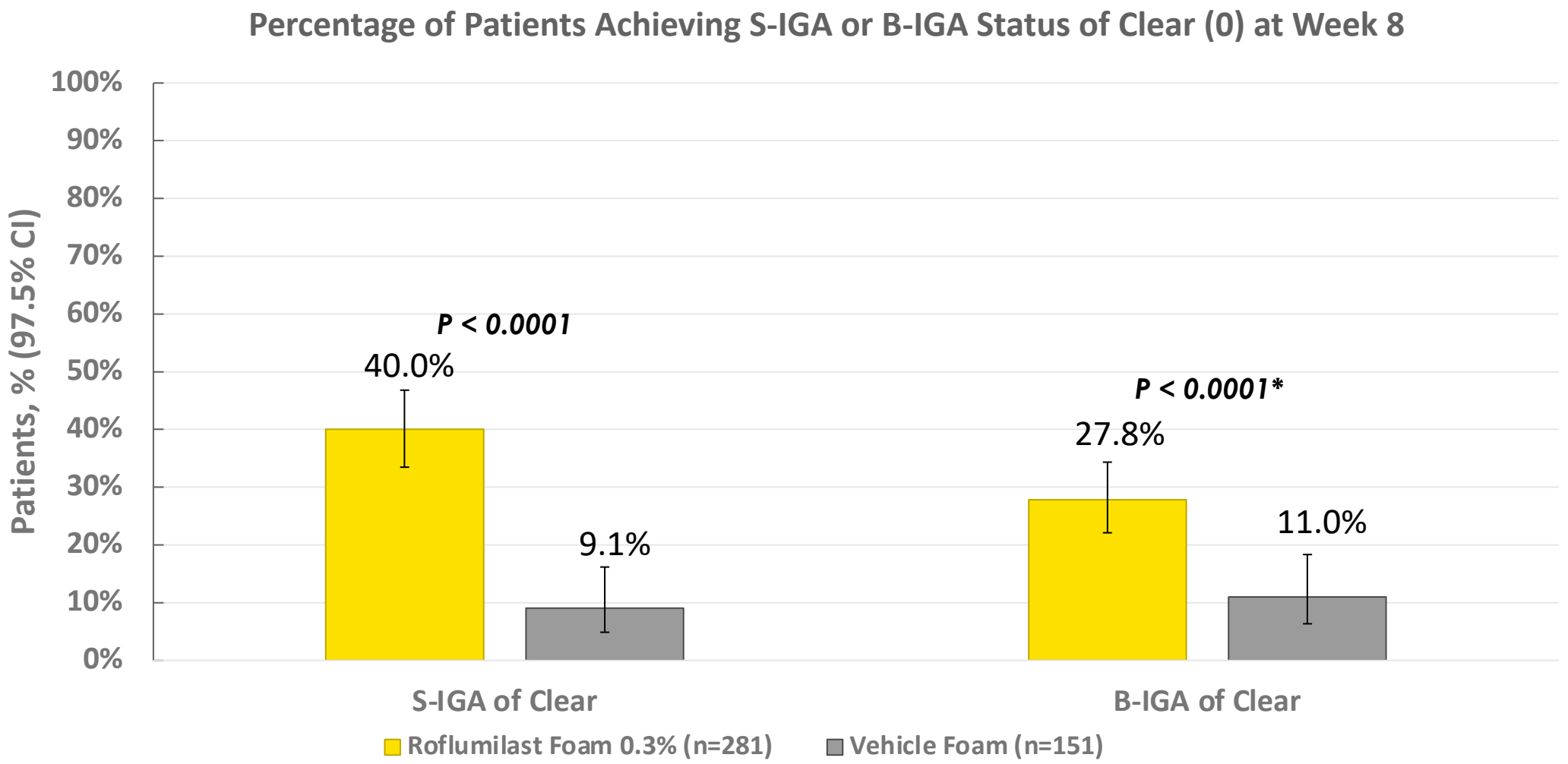
Patients, n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle (n=151)
Psoriasis Involvement in the Following Areas at Screening		
Elbows	182 (64.8)	103 (68.2)
Genitalia	47 (16.7)	28 (18.5)
Knees	123 (43.8)	54 (35.8)
Face	98 (34.9)	59 (39.1)
Elbows or knees	199 (70.8)	109 (72.2)
Scalp and Body Psoriasis specific Medical History		
Prior Topical Corticosteroid Use	299 (81.5)	125 (82.8)
Prior Inadequate Response, Intolerance, or Contraindication	165 (58.7)	88 (58.3)
Prior Topical Vitamin D Derivative Use	50 (17.8)	27 (17.9)
Prior Inadequate Response, Intolerance, or Contraindication	36 (12.8)	17 (11.3)

Improvement in Scalp and Body Psoriasis at Week 8



B-IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline; . S-IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline.
B-IGA: Body-Investigator Global Assessment; CI: confidence interval; PASI: Psoriasis Area and Severity Index; PASI-75: 75% reduction in PASI; S-IGA: Scalp-Investigator Global Assessment. .

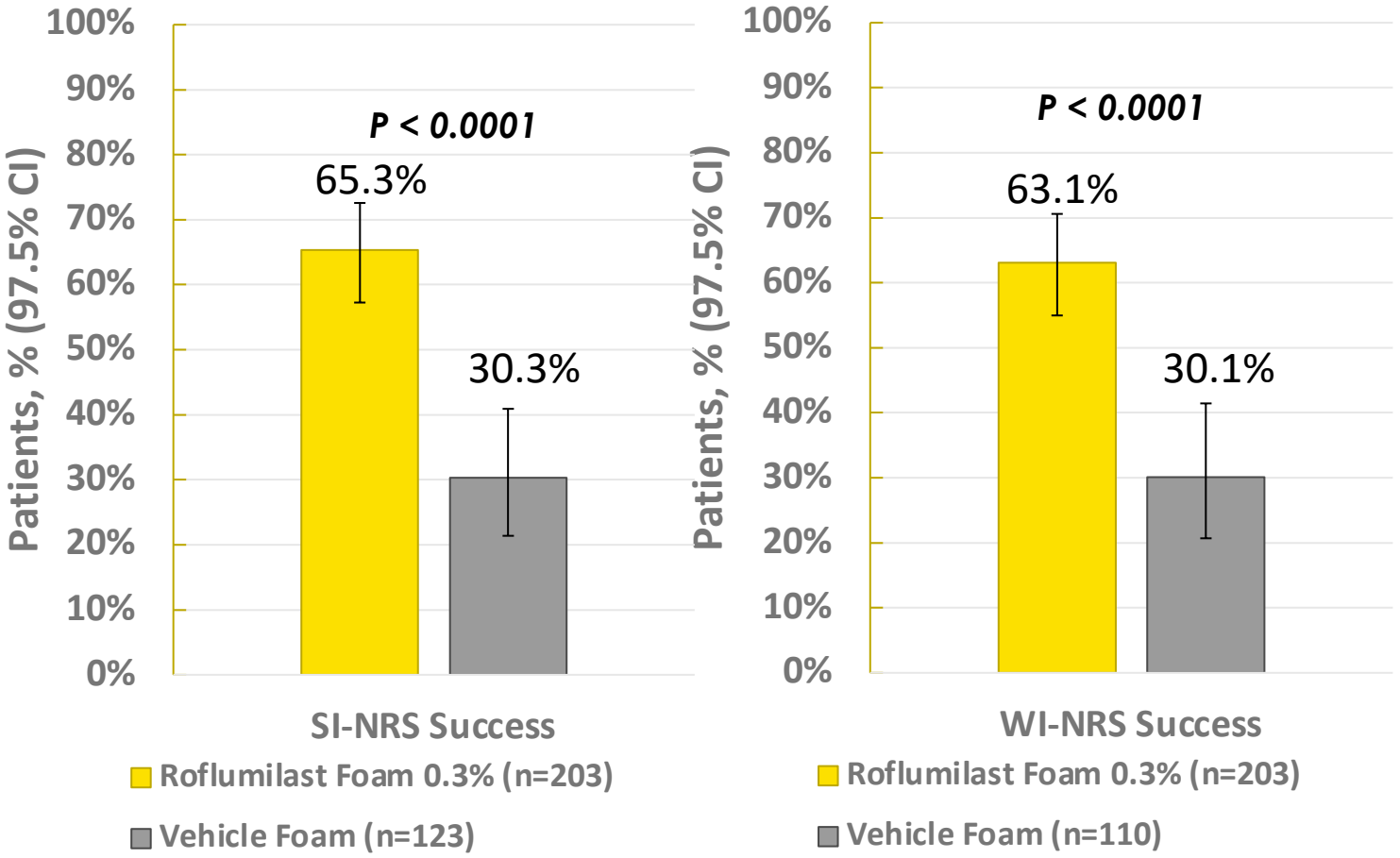
Clearance of Scalp and Body Psoriasis at Week 8



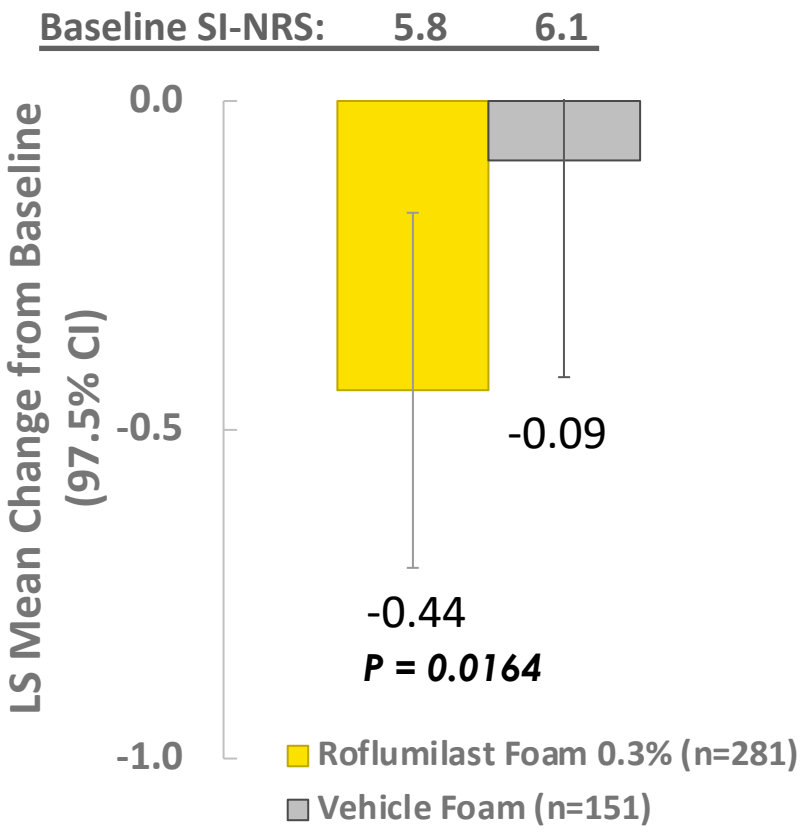
*Nominal P-value.
B-IGA: Body-Investigator Global Assessment; CI: confidence interval; S-IGA: Scalp-Investigator Global Assessment.

Improvement in Scalp and Body Pruritus

SI-NRS and WI-NRS Success at Week 8



SI-NRS 24 hours after the first application

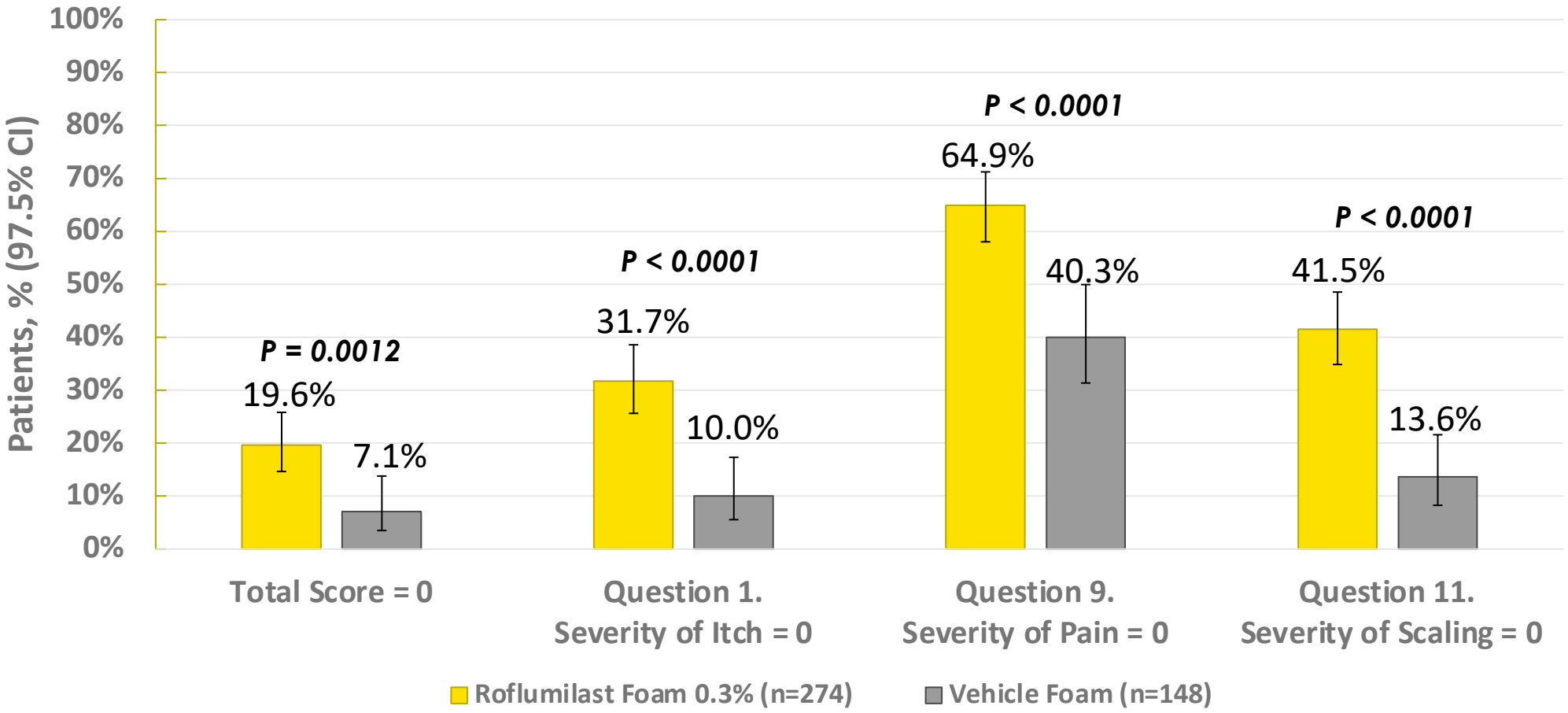


SI-NRS Success: achievement of ≥4-point improvement from baseline in patients with baseline SI-NRS ≥4; WI-NRS Success: achievement of ≥4-point improvement from baseline in patients with baseline WI-NRS ≥4;
CI: confidence interval; LS, least squares; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Improvement in Patient Quality of Life at Week 8

Percentage of patients achieving a Score of 0 on the Psoriasis Symptom Diary (PSD) at Week 8

PSD: Psoriasis-related severity and burden in the past 24 hours



CI, confidence interval; PSD, psoriasis symptom diary

The PSD is a 16-item questionnaire asking subjects to rate the severity and burden of psoriasis-related symptoms in the past 24 hours. Each question is scored from 0 (no symptoms) to 10 (worst imaginable symptoms) Total PSD Scores range from 0-160.

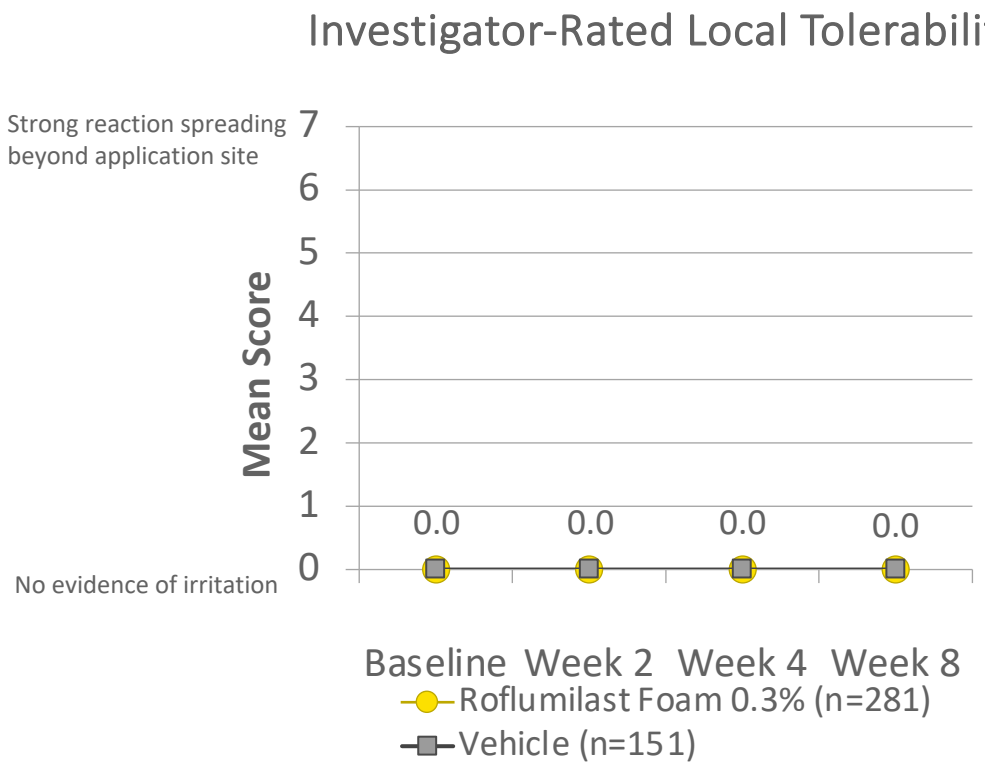
Overall Adverse Events

n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle (n=151)
Patients with any TEAE	75 (26.7)	25 (16.6)
Patients with any treatment-related TEAE	16 (5.7)	3 (2.0)
Patients with any treatment-emergent SAE	2 (0.7)	1 (0.7)
Patients with any treatment-related SAE	1 (0.4)	0
Patients who discontinued study drug due to AE	7 (2.5)	2 (1.3)
Patients who discontinued study due to TEAE	5 (1.8)	2 (1.3)
Most common TEAEs by preferred term, ≥1% in any group		
Headache	13 (4.6)	3 (2.0)
Diarrhea	9 (3.2)	4 (2.6)
COVID-19	8 (2.8)	4 (2.6)
Nausea	6 (2.1)	0
Nasopharyngitis	4 (1.4)	2 (1.3)
Hypertension	3 (1.1)	2 (1.3)
Upper respiratory tract infection	3 (1.1)	0
Urinary tract infection	2 (0.7)	2 (1.3)

SAEs include bipolar disorder (roflumilast; unrelated), gastritis (roflumilast; possibly related), joint dislocation, peripheral artery occlusion and radius fracture (vehicle; all unrelated).
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Local Tolerability Assessments

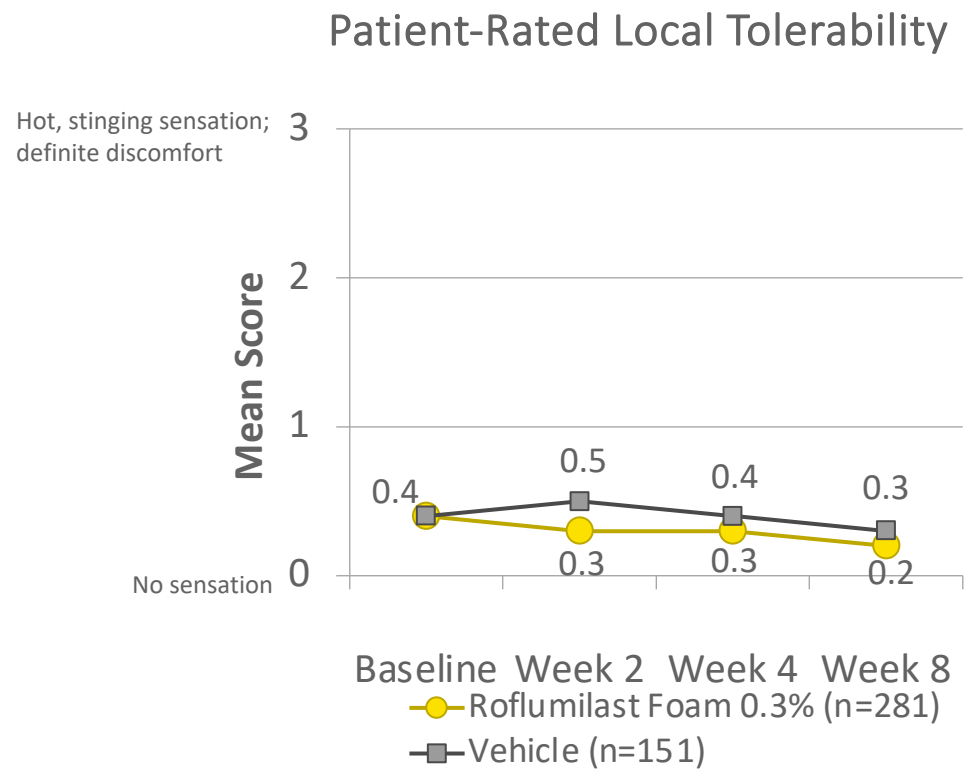
100% of roflumilast-treated and vehicle-treated patients had no evidence of irritation



Scale for investigator-rated local tolerability (0-7)

0 = no evidence of irritation; 1 = minimal erythema, barely perceptible; 2 = definite erythema, readily visible; minimal edema or minimal papular response; 3 = erythema and papules; 4 = definite edema; 5 = erythema, edema and papules; 6 = vesicular eruption; 7 = strong reaction spreading beyond application site

≥95% of patients had reported "no sensation" or "slight warm, tingling sensation; not really bothersome"



Scale for patient-rated local tolerability (0-3)

0 (none)= no sensation; 1 (mild) = slight warm, tingling sensation; not really bothersome; 2 (moderate) = definite warm, tingling sensation that is somewhat bothersome; 3 (severe) = hot, tingling/stinging sensation that has caused definite discomfort

Conclusions

- Once-daily, nonsteroidal roflumilast foam 0.3% provided improvement across multiple efficacy endpoints versus vehicle in patients with scalp and body psoriasis:
  - Significant improvement in scalp itch was observed as early as 24 hours after first application of roflumilast foam 0.3%
- Efficacy outcomes were reflected in patients-reported outcomes
  - Significantly more patients treated with roflumilast foam achieved a PSD score of 0 than vehicle
  - Significant improvement in patient-reported scaling, itch, and pain
- Safety and local tolerability were favorable
  - Low rates of adverse events and discontinuations due to adverse events, generally similar to vehicle
- These results are consistent with the outcomes observed with roflumilast cream 0.3% in patients with psoriasis[1]

PSD, Psoriasis Symptom Diary.

1. Lebwohl M et al. JAMA. 2022;328:1073-1084.