Efficacy and safety of roflumilast foam 0.3% in patients with seborrheic dermatitis in a phase 3 trial

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Introduction

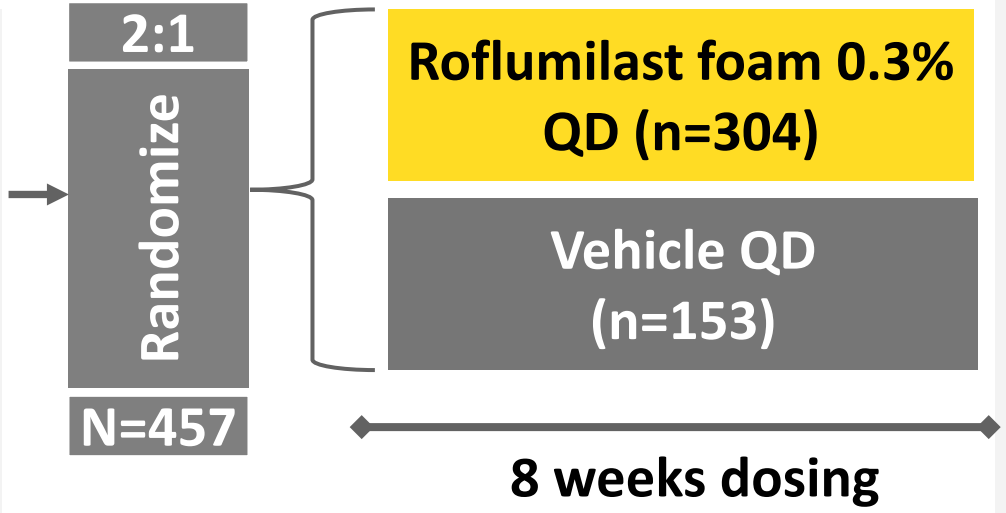
- Seborrheic dermatitis (SD) is a common, chronic, inflammatory skin disease that affects patients of all ages, with a global prevalence of approximately 5%[1]
- Treatment is via topical therapies, including antifungal agents and corticosteroids, which have limitations (side effects and/or inability to use on both hair-/non-hair bearing areas)
- Roflumilast is a selective phosphodiesterase 4 (PDE4) inhibitor with greater affinity for PDE4 than apremilast and crisaborole (25- to >300-fold more potent in *in vitro* assays)[4]
- Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for long-term management of psoriasis (FDA-approved July 29, 2022), atopic dermatitis, and SD
- Efficacy, safety, and tolerability of roflumilast foam have been demonstrated in a phase 2a trial in SD[5] and a subsequent open-label safety trial (NCT04091646/NCT04445987)
- Here, we report the results of a phase 3 trial (NCT04973228) of roflumilast foam 0.3% in patients with SD

1. Dessinioti and Katsambas. Clin Dermatol. 2013;31:343-351. 2.Tucker D, Masood S. StatPearls Publishing; 2021. 3. Adalsteinsson JA, et al. *Exp Dermatol.* 2020;29(5):481-489. 4. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
5. Zirwas M, et al. European Academy of Dermatology and Venereology (EADV) Congress 2021.

Trial Design: Phase 3, Randomized, Parallel-group, Double-blind, Vehicle-controlled Study

Eligibility

- Diagnosis of at least moderate seborrheic dermatitis (IGA ≥3)
- Age ≥9
- ≤20% BSA



Endpoints[a]

- Primary: IGA Success (0 or 1 With a 2-Grade Improvement) at Week 8
- Secondary:
  - IGA Success at Weeks 2 and 4
  - IGA of Clear at Week 8
  - WI-NRS at Weeks 2, 4, and 8
  - Erythema Score of 0 at Week 8
  - Scaling Score of 0 at Week 8
- Safety & tolerability

*As this study is a single pivotal trial, the statistical significance of the primary endpoint was assessed at the 1% significance level (2-sided). To control for multiple testing, the 1% alpha was partitioned to .0033 for WI-NRS endpoints and .0067 for other secondary endpoints

AE: adverse event; BSA: body surface area; IGA: Investigator Global Assessment; QD: once daily; SAE: serious adverse event; SD: seborrheic dermatitis; WI-NRS: Worst Itch Numeric Rating Scale.

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Baseline Demographics

	Roflumilast Foam 0.3% (n=304)	Vehicle (n=153)
Age in years, mean (SD)	43.2 (16.8)	41.8 (17.5)
Sex		
Male, n (%)	153 (50.3)	75 (49.0)
Female, n (%)	151 (49.7)	78 (51.0)
Race, n (%)		
American Indian or Alaska Native	4 (1.3)	0
Asian	18 (5.9)	10 (6.5)
Black or African American	36 (11.8)	15 (9.8)
Native Hawaiian or Other Pacific Islander	0	1 (0.7)
White	234 (77.0)	122 (79.7)
More than 1 race	1 (0.3)	1 (0.7)
Other	11 (3.6)	4 (2.6)
Ethnicity		
Hispanic or Latino	69 (22.7)	28 (18.3)
Not Hispanic or Latino	235 (77.3)	125 (81.7)

SD: standard deviation

Baseline Disease Characteristics

	Roflumilast Foam 0.3% (n=304)	Vehicle (n=153)
IGA score, n (%)		
3 (moderate)	287 (94.4)	141 (92.2)
4 (severe)	17 (5.6)	12 (7.8)
Erythema score, n (%)		
2 (mild)	0	1 (0.7)
3 (moderate)	282 (92.8)	141 (92.2)
4 (severe)	22 (7.2)	11 (7.2)
Scaling score, n (%)		
2 (mild)	0	0
3 (moderate)	256 (84.2)	130 (85.0)
4 (severe)	48 (15.8)	23 (15.0)
WI-NRS, mean score (Std Dev)	5.06 (2.34)	4.74 (2.29)
WI-NRS score ≥4, n (%)	206 (67.8)	98 (64.1)
BSA, mean % (Std Dev)	2.89 (2.03)	2.98 (2.57)

BSA: body surface area; IGA: Investigator Global Assessment; Std Dev: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Baseline Disease Characteristics: Body Areas Involved

Patients, n (%)	Roflumilast Foam 0.3% (n=304)	Vehicle(n=153)
Scalp	291 (95.7)	136 (88.9)
Face	186 (61.2)	98 (64.1)
Eyelids Involved	29 (9.5)	13 (8.5)
Ears	146 (48.0)	79 (51.6)
Neck	33 (10.9)	13 (8.5)
Trunk	28 (9.2)	18 (11.8)
Other	11 (3.6)	4 (2.6)

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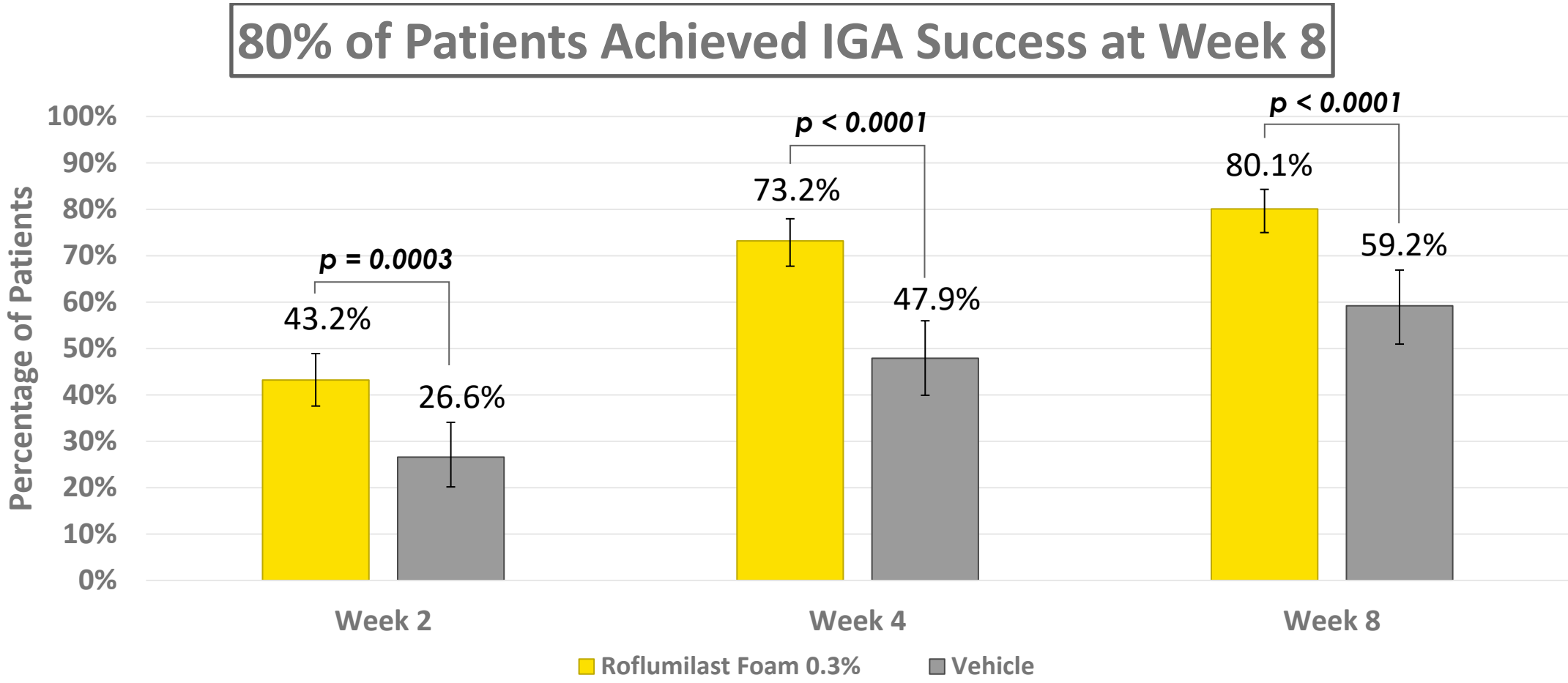
Significantly More Roflumilast-treated Patients Achieved IGA Success (0/1 With ≥2-Grade Improvement)



IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline
Intent-to-treat population; missing scores imputed using multiple imputations
Error bars represent 95% confidence interval
Statistical significance was concluded at the 1% significance level (2-sided).
IGA: Investigator Global Assessment.

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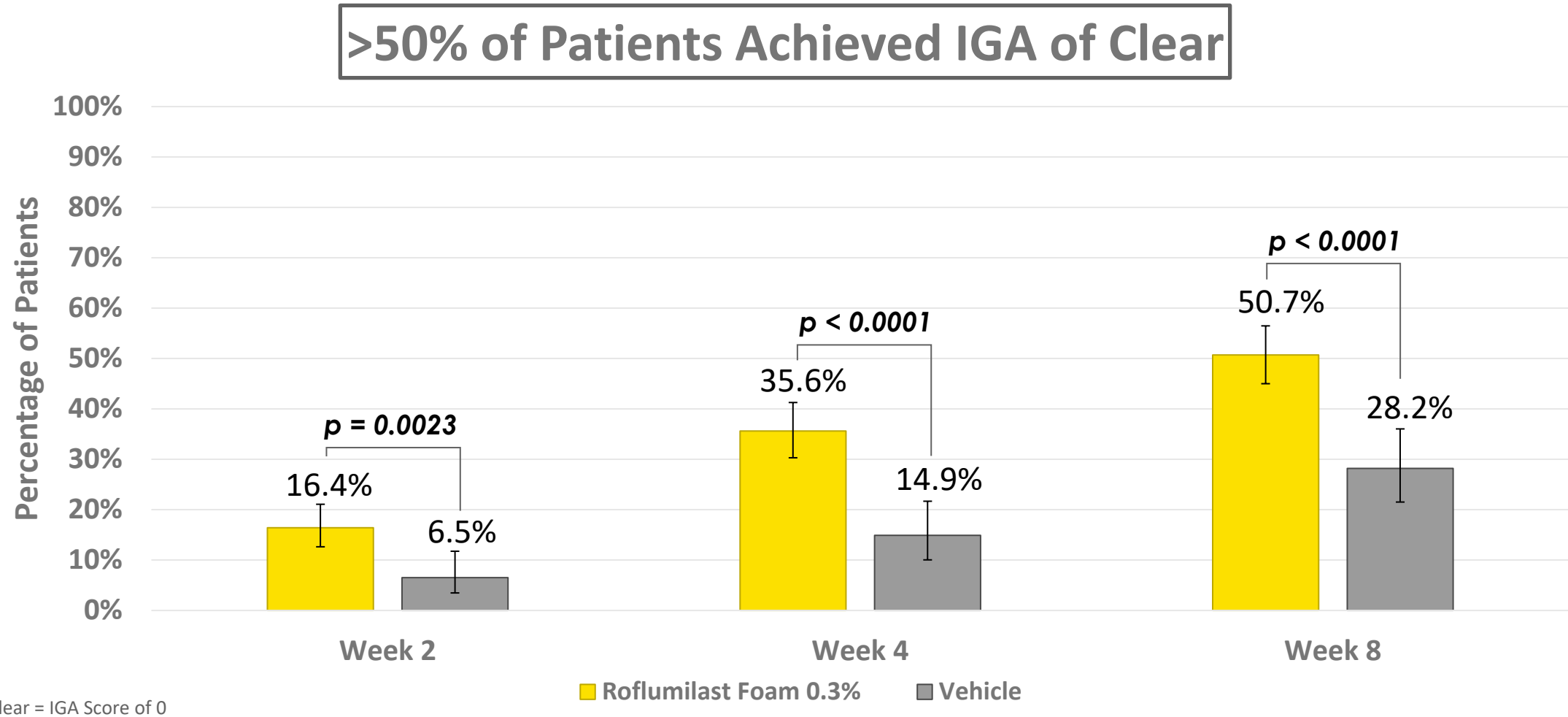
Significantly More Roflumilast-treated Patients Achieved IGA Status of Clear (0)



IGA Clear = IGA Score of 0
Intent-to-treat population; missing scores imputed using multiple imputations, p-values are not adjusted for multiple testing
Error bars represent 95% confidence interval
IGA: Investigator Global Assessment.

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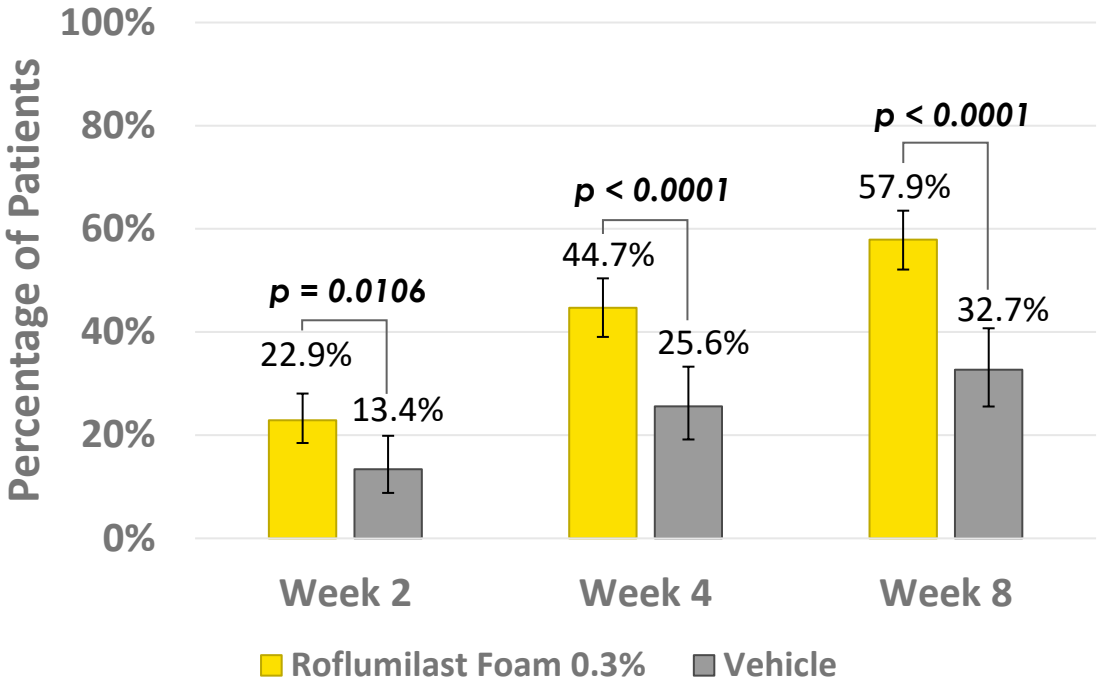
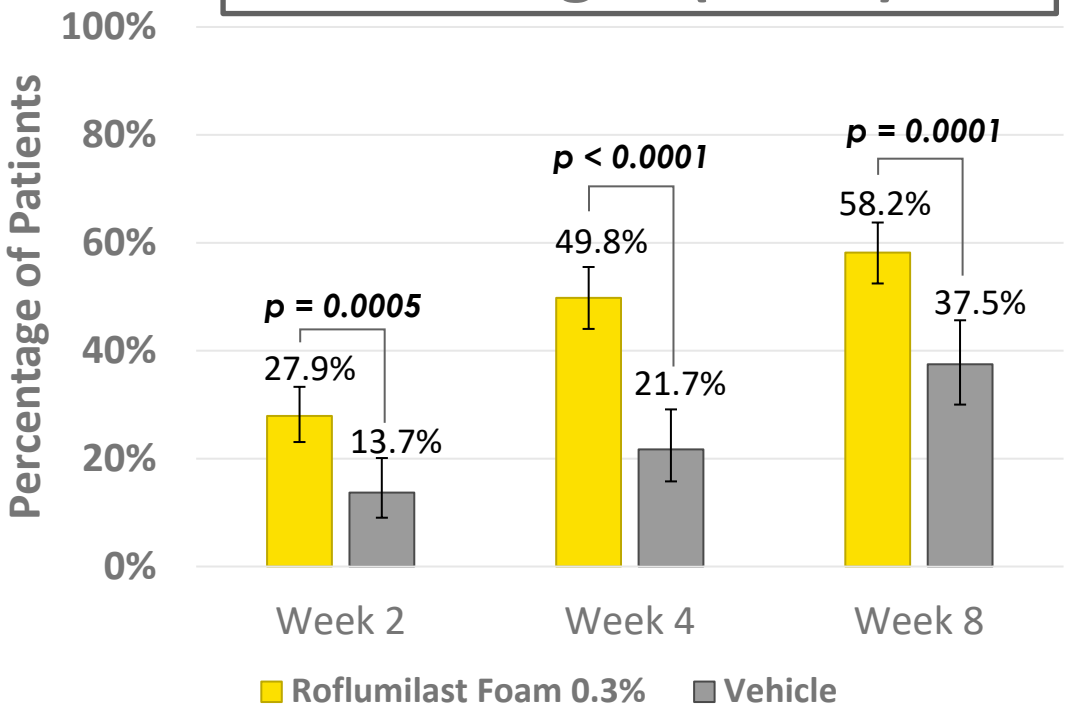
Significantly More Roflumilast-treated Patients Achieved Erythema and Scaling Scores of 0 at Week 8

>50% of Patients Achieved Erythema=0 (None)



>50% of Patients Achieved Scaling=0 (None)



Intent-to-treat population; missing scores imputed using multiple imputations
Error bars represent 95% confidence interval
Evaluated at α=0.0067

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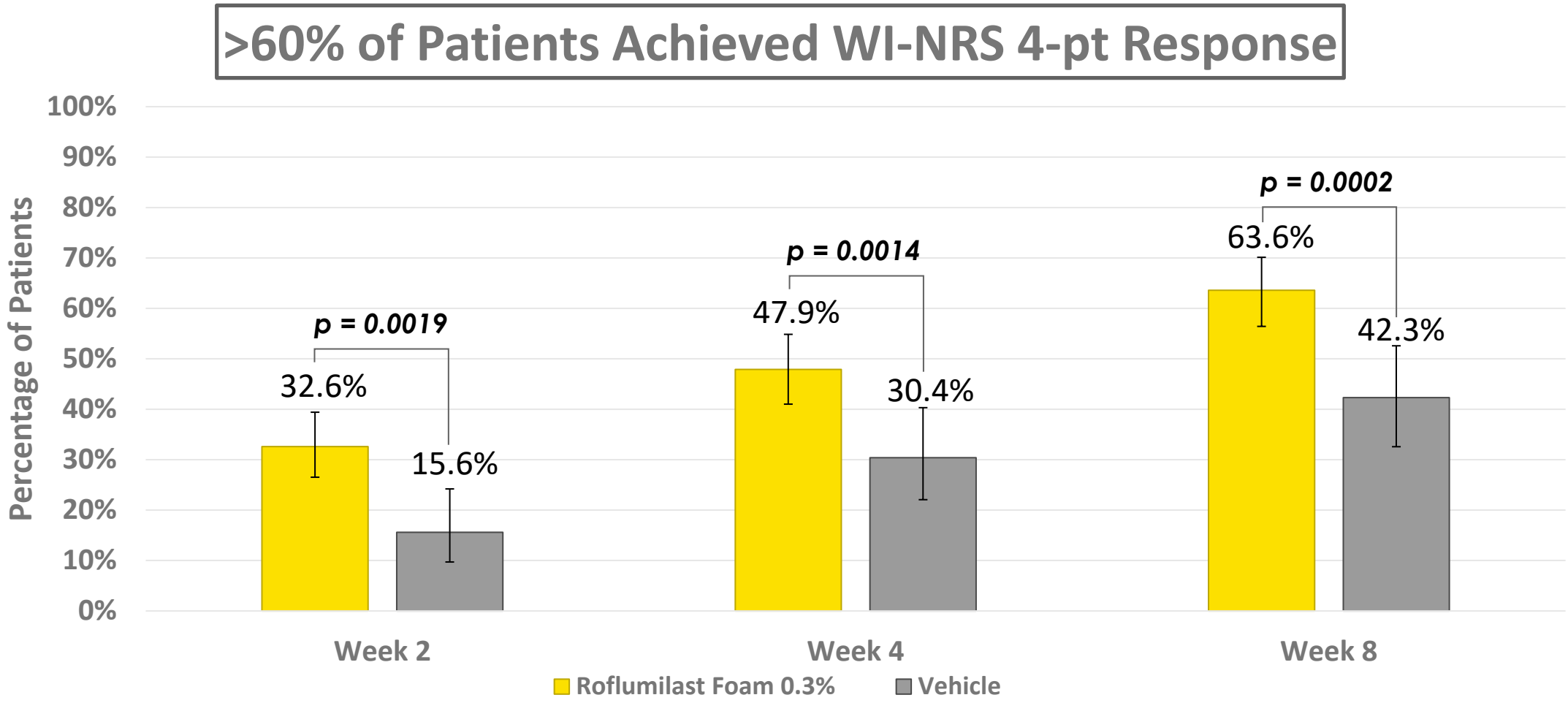
Significantly More Roflumilast-treated Patients Achieved WI-NRS Success



Missing scores imputed using multiple imputations
Error bars represent 95% confidence interval
WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4; evaluated at α=0.0033.
WI-NRS: Worst Itch Numeric Rating Scale.

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Adverse Events

n (%)	Roflumilast Foam 0.3% (n=304)	Vehicle (n=153)
Patients with any TEAE	70 (23.0)	33 (21.6)
Patients with any treatment-related TEAE	8 (2.6)	5 (3.3)
Patients with any treatment-emergent SAE*	1 (0.3)	0
Patients who discontinued study due to AE†	2 (0.7)	3 (2.0)
Most common TEAE (>1% in any group), preferred term‡		
COVID-19	11 (3.6)	5 (3.3)
Urinary tract infection	4 (1.3)	3 (2.0)
Nausea	5 (1.6)	0
Nasopharyngitis	4 (1.3)	1 (0.7)
Application site pain	1 (0.3)	3 (2.0)
Sinusitis	0	2 (1.3)

*Keratoacanthoma, not in application site, deemed unrelated

†Reasons for discontinuation in the roflumilast-treated group includes diarrhea/hematochezia/abdominal pain in one patient with a past history of Crohn's and decreased potassium in the second patient

‡Presented in descending order for overall rates.

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

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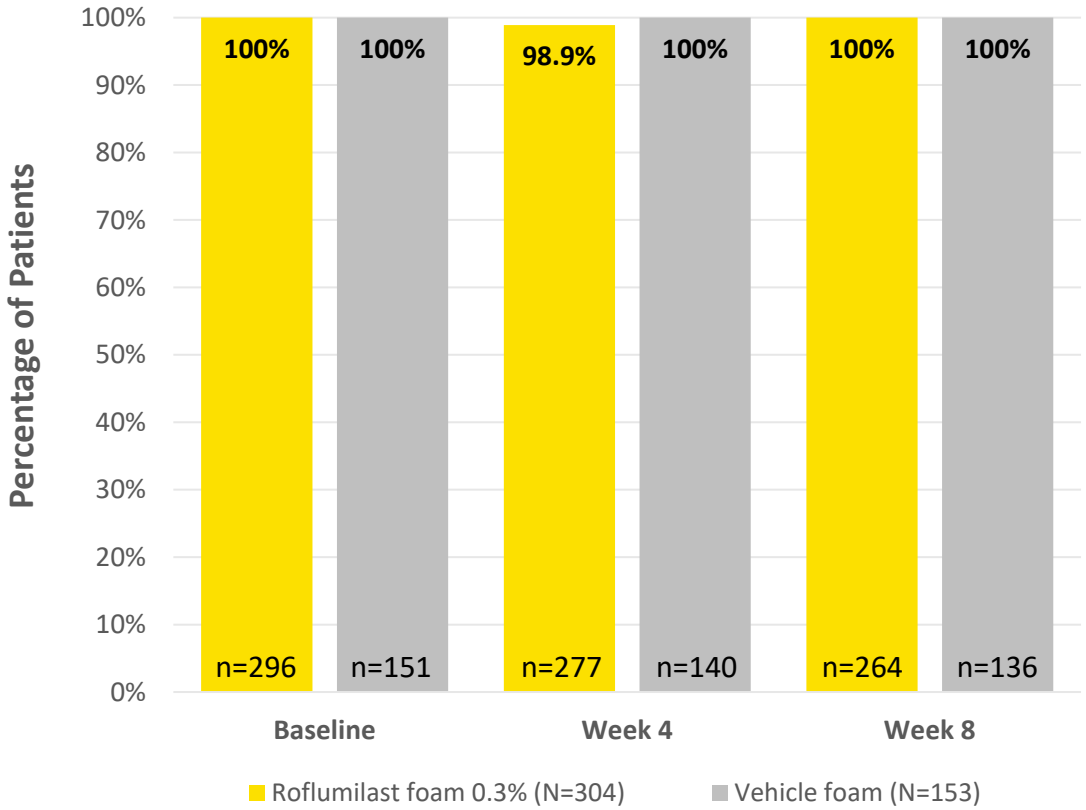
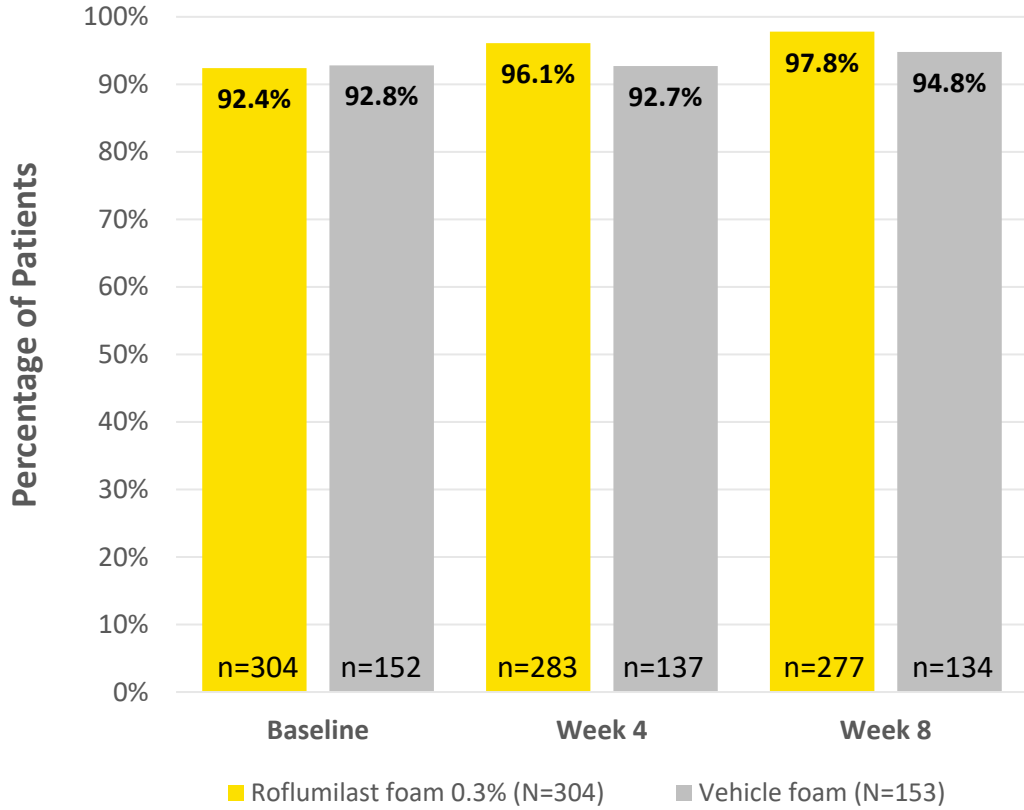
Local Tolerability Assessments (Safety Population)
Patient-rated and Investigator-rated

Investigator-rated Local Tolerability
% Patients with No Signs of Irritation



Patient-rated Local Tolerability
% Patients with No or Mild Sensation



*Scale for investigator-rated local tolerability: 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[1]

†Scale for patient-rated local tolerability: 0 = no sensation; 1 = slight warm, tingling sensation; not really bothersome; 2 = definite warm, tingling sensation that is somewhat bothersome; 3 = hot, tingling/stinging sensation that has caused definite discomfort

1. Berger and Bowman. J Toxicol: Cut Ocular Toxicol. 1982;1:109-115.

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Conclusions

- **Once-daily, non-steroidal roflumilast foam 0.3% provided improvement across multiple efficacy endpoints vs. vehicle in patients with SD in a Phase 3 trial**
  - ***80% of patients achieved IGA Success and >50% achieved complete clearance by Week 8***
  - ***>60% of patients achieved an itch response at Week 8, with significant improvements at the 2- and 4-week assessments***
- **Local tolerability was highly favorable as reported by patient and investigator assessments of irritation, burning, and stinging, consistent with safety profiles in prior trials**

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