Efficacy and Safety of Roflumilast Foam 0.3% in Patients With Seborrheic Dermatitis in a Phase 3 Trial

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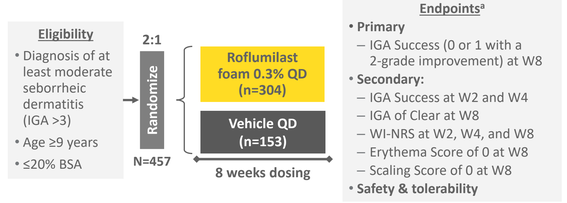
INTRODUCTION

- 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)[2]
- 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[3] 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

METHODS

- This phase 3 randomized, parallel-group, double-blind, vehicle-controlled trial was conducted in patients ≥9 years old with at least moderate SD affecting scalp and/or non-scalp areas (**Figure 1**)
- The primary efficacy endpoint was Investigator Global Assessment (IGA) Success (IGA of Clear or Almost Clear plus ≥2-grade improvement from baseline) at Week 8

Figure 1. Study Design



[a]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 0.0033 for WI-NRS endpoints and 0.0067 for other secondary endpoints.
BSA: body surface area; IGA: Investigator Global Assessment; QD: once daily; W: week; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

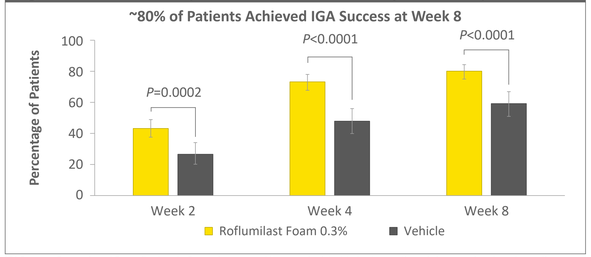
- Baseline patient demographics and disease characteristics were similar between the groups (**Table 1**)
- Overall, significantly more roflumilast-treated patients than vehicle-treated patients achieved the primary efficacy endpoint of IGA Success (**Figure 2**) and IGA status of Clear (**Figure 3**) at Week 8
  - Percentages of patients achieving IGA Success and IGA Clear at Weeks 2 and 4 were also greater with roflumilast
- Significantly greater percentages of roflumilast- than vehicle-treated patients achieved secondary endpoints of:
  - WI-NRS Success at Weeks 2, 4, and 8 (**Figure 4**)
  - Overall Assessment of Erythema score of 0 (**Figure 5**) at Week 8
  - Overall Assessment of Scaling score of 0 (**Figure 5**) at Week 8
- Local tolerability was favorable on investigator- and patient-rated assessments (**Figure 6**)
- Overall incidence of treatment-emergent adverse events (TEAEs), serious adverse events, and TEAEs leading to discontinuation were low, with similar rates between roflumilast and vehicle (**Table 2**)

Table 1. Baseline Demographics and Disease Characteristics

	Roflumilast Foam 0.3% (n=304)	Vehicle (n=153)
Age in years, mean (Std Dev)	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, n (%)		
Hispanic or Latino	69 (22.7)	28 (18.3)
Not Hispanic or Latino	235 (77.3)	125 (81.7)
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)
Scalp, n (%)	291 (95.7)	136 (88.9)
Face, n (%)	186 (61.2)	98 (64.1)
Eyelids involved, n (%)	29 (9.5)	13 (8.5)
Ears, n (%)	146 (48.0)	79 (51.6)
Neck, n (%)	33 (10.9)	13 (8.5)
Trunk, n (%)	28 (9.2)	18 (11.8)
Other, n (%)	11 (3.6)	4 (2.6)

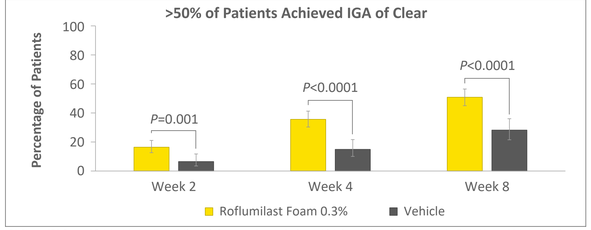
BSA: body surface area; IGA: Investigator Global Assessment; Std Dev: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 2. IGA Success (0 or 1 With a 2-Grade Improvement)



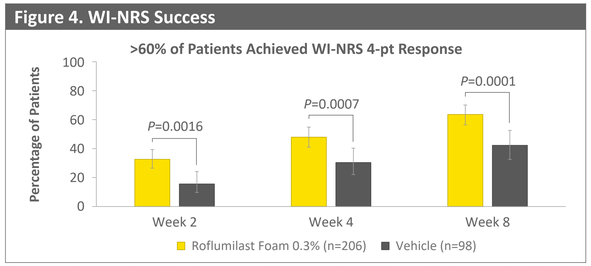
IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline Intent-to-treat population; missing scores imputed using multiple imputations. Error bars represent 95% confidence interval. Statistical significance was concluded at the 1% significance level (2-sided).
IGA: Investigator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

Figure 3. IGA Status of Clear (0)



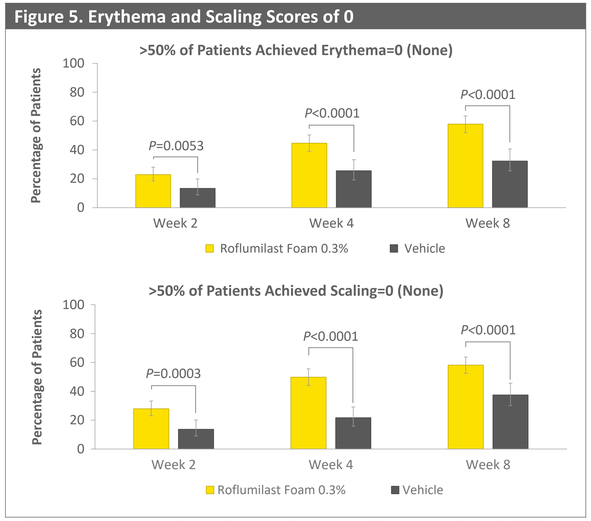
IGA Clear = IGA Score of 0. Intent-to-treat population; missing scores imputed using multiple imputations, *P*-values are not adjusted for multiple testing. Error bars represent 95% confidence interval.
IGA: Investigator Global Assessment.

Figure 4. 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.

Figure 5. Erythema and Scaling Scores of 0



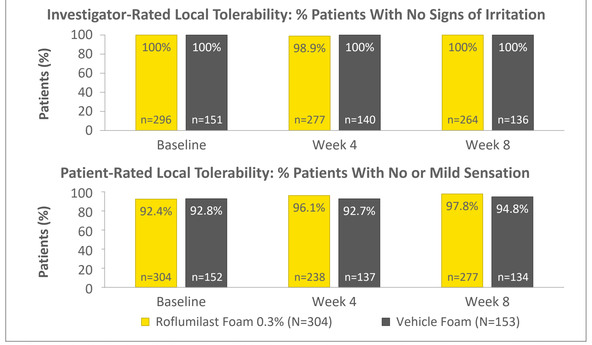
Intent-to-treat population; missing scores imputed using multiple imputations. Error bars represent 95% confidence interval. Evaluated at α=0.0067.

Table 2. 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[a]	1 (0.3)	0
Patients who discontinued study due to AE[b]	2 (0.7)	3 (2.0)
Most common TEAE (>1% in any group), preferred term[c]		
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)

[a]Keratoacanthoma, not in application site, deemed unrelated. [b]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. [c]Presented in descending order for overall rates.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Figure 6. Local Tolerability Assessments (Safety Population)



[a]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. [b]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.

CONCLUSIONS

- Once-daily, nonsteroidal roflumilast foam 0.3% provided improvement across multiple efficacy endpoints versus 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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DISCLOSURES

AB, JA-L, NB, AB, ZDD, JD, SBF, MG, STG, AAH, EL, AYM, KAP, LSG, and **MZ** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **SK, DK, PB, DHC,** and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.