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

Andrew Blauvelt,[1] Zoe D. Draelos,[2] Melinda Gooderham,[3] Edward Lain,[4] Angela Y. Moore,[5] Kim A. Papp,[6] Matthew Zirwas,[7] David Krupa,[8] Patrick Burnett,[8] David R. Berk,[8] David H. Chu[8]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]Dermatology Consulting Services, High Point, NC, USA; [3]SKiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [4]Sanova Dermatology, Austin, TX, USA; [5]Arlington Research Center, Arlington, TX, and Baylor University Medical Center, Dallas, TX, USA; [6]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [7]Dermatologists of the Central States, Probity Medical Research, and Ohio University, Bexley, OH, USA; [8]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

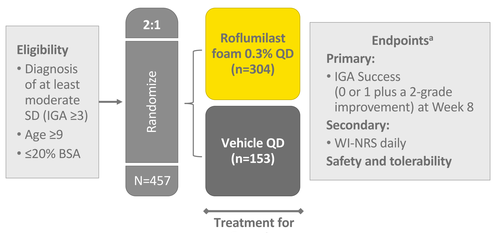
INTRODUCTION

- Seborrheic dermatitis (SD) is a chronic inflammatory skin condition that negatively impacts quality of life, particularly in patients with more severe disease[1]
  - Itch is a major complaint among patients with SD[2]
- Topical treatments include antifungals, steroids, immunomodulators, and dandruff shampoos,[3,4] but efficacious and safe options are needed, especially those that improve itch
- Roflumilast is a selective, potent, phosphodiesterase 4 inhibitor being investigated as a once-daily foam for treatment of SD[5]

METHODS

- This phase 3, randomized, parallel-group, double-blind, vehicle-controlled trial (NCT04973228) was conducted in patients ≥9 years old with at least moderate SD affecting scalp and/or non-scalp areas
- Eligible patients had clinical diagnosis of SD of ≥3-month duration, Investigator Global Assessment (IGA) score ≥3 (at least moderate severity), and affecting ≤20% of the body surface area (BSA; **Figure 1**)
- Patients were randomized 2:1 to apply once-daily roflumilast foam 0.3% (n=304) or vehicle (n=153) for 8 weeks
- The primary efficacy endpoint was IGA Success (Completely Clear/Almost Clear [score 0–1] plus ≥2-grade improvement) at Week 8
  - Secondary efficacy endpoints included Worst Itch Numeric Rating Scale (WI-NRS), which was completed daily by patients
- Safety and local tolerability were also evaluated

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; SD: seborrheic dermatitis; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

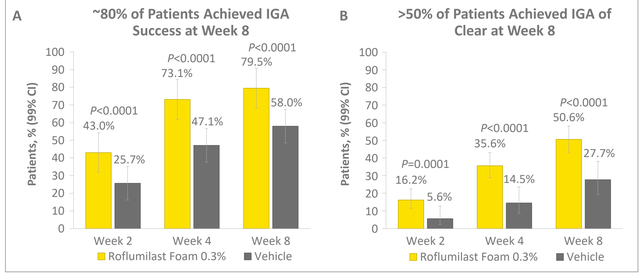
- Demographics and baseline characteristics were similar in the treatment groups (**Table 1**)
- Overall, significantly more roflumilast-treated patients than vehicle-treated patients achieved IGA success (79.5% vs 58.0%; *P*<0.0001) and IGA status of Clear (50.6% vs 27.7%; *P*<0.0001) at Week 8 (**Figure 2**)
- Significantly greater percentages of roflumilast- than vehicle-treated patients had ≥4-point improvement on WI-NRS at Weeks 2 (32.7% vs 15.5%; *P*=0.0005), 4 (47.6% vs 29.1%%; *P*=0.0003), and 8 (62.8% vs 40.6%; *P*<0.0001; **Figure 3**)
- Greater improvement in itch was observed among roflumilast-treated patients as early as 48 hours after the first application (mean percent change from baseline: -27.87% vs -13.11%; nominal *P*=0.0024; **Figure 4**)
- Changes in SD in patients treated with roflumilast foam 0.3% are shown in **Figure 5**

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		
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)
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)

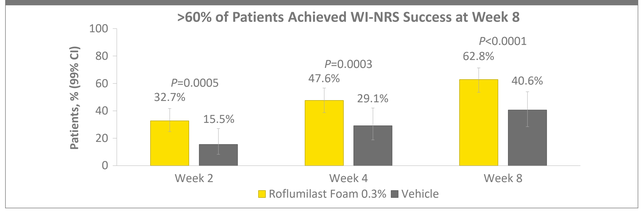
BSA: body surface area; IGA: Investigator Global Assessment; Std Dev: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 2. Patients Achieving IGA Success and IGA Clear



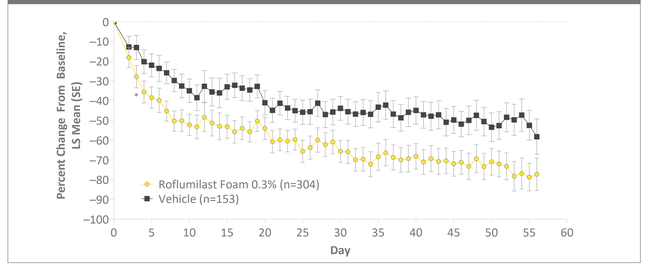
IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline. Intent-to-treat population; missing scores imputed using multiple imputations. Error bars represent 99% confidence interval. Statistical significance was concluded at the 1% significance level (2-sided). IGA Clear = IGA score of 0. *P*-values are not adjusted for multiple testing.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Percentage of Patients Achieving WI-NRS Success



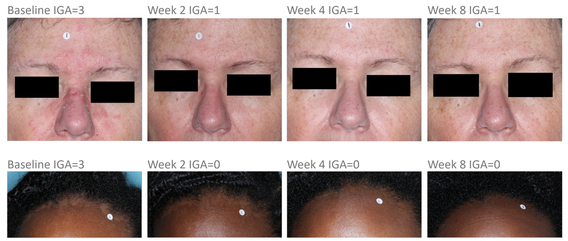
Missing scores imputed using multiple imputations. Error bars represent 99% confidence intervals. WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4; evaluated at α=0.0033.
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 4. LS Percent Change in Daily WI-NRS Scores



*P=0.0024 at 48 hours after dosing and P<0.05 for difference from vehicle for all timepoints assessed after. Observed data, intent-to-treat population.
LS: least squares; SE: standard error; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 5. Changes in SD in Patients Treated With Roflumilast Foam 0.3%



IGA: Investigator Global Assessment; SD: seborrheic dermatitis.

Safety

- Rates of adverse events (AEs) with roflumilast foam and vehicle foam were low (**Table 2**)
  - Few treatment-related AEs were reported
  - Very few AEs led to study discontinuation, with similar rates of discontinuation between roflumilast and vehicle groups
  - Only 1 patient had a serious AE, and it was considered unrelated to treatment

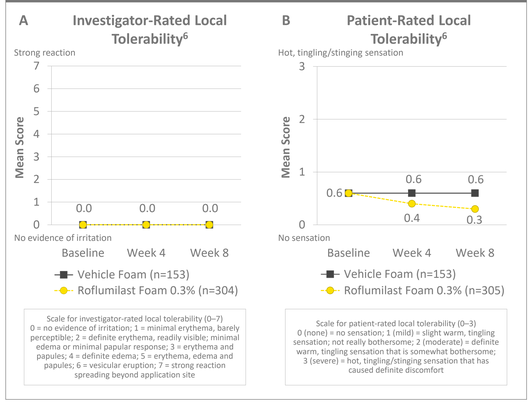
Table 2. Overall AEs

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.

- Roflumilast foam was well-tolerated (**Figure 6**)
  - ≥98.9% of roflumilast-treated and 100% of vehicle-treated patients had no evidence of irritation on the investigator-rating of local tolerability
  - ≥92.4% of patients had reported "no sensation" or "slight warm, tingling sensation; not really bothersome" on the patient-rated assessment of local tolerability

Figure 6. Local Tolerability Assessments (Safety Population)



CONCLUSIONS

- Once-daily, non-steroidal roflumilast foam 0.3% provided improvement across multiple efficacy endpoints, including rapid itch improvement, 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
  - Greater improvement in daily itch scores was observed among roflumilast-treated patients as early as 48 hours after first dose
- Local tolerability was highly favorable on investigator- and patient-rated assessments and was consistent with safety profiles in prior trials

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DISCLOSURES

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