Roflumilast Foam 0.3% Once Daily in Patients With Seborrheic Dermatitis: Improvement in Patient-Reported Outcomes and Pruritus From a Phase 3 Trial (STRATUM)

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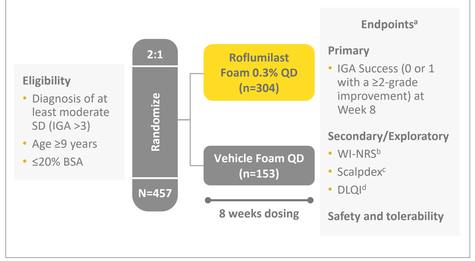
INTRODUCTION

- Seborrheic dermatitis (SD) is a common chronic inflammatory skin condition that has a significant negative impact on patients' quality of life[1]
  - In a survey of 300 patients with SD, patients reported SD caused a measurable impact on their day-to-day life, self-esteem, and multiple aspects of their mental health, causing anxiety and depression[2]
  - Furthermore, the majority of patients reported SD negatively impacted their ability to do their job, with almost half of patients having ever missed work due to SD symptoms[2]
- Roflumilast is a potent phosphodiesterase 4 (PDE4) inhibitor formulated as a water-based cream and foam
  - Roflumilast potency is ~25- to >300-fold higher than apremilast and crisaborole, with roflumilast more closely mimicking cyclic adenosine monophosphate (cAMP) binding to PDE4[3,4]
  - Formulations do not contain ethanol, propylene glycol, or fragrances that can irritate skin
- Roflumilast foam 0.3% demonstrated favorable efficacy, safety, and tolerability in the Phase 3 clinical trial in patients with moderate to severe SD (STRATUM; NCT04973228)[5]
  - Here, we report results for patient-reported outcomes from STRATUM

METHODS

- STRATUM was a Phase 3, randomized, parallel-group, double-blind, vehicle-controlled trial enrolling patients ≥9 years of age with at least moderate SD affecting scalp and/or non-scalp areas (Figure 1)
  - The primary efficacy endpoint was Investigator Global Assessment Success (IGA of Clear or Almost Clear plus ≥2-grade improvement from baseline) at Week 8
  - Patient-reported outcomes included Worst Itch Numeric Rating Scale (WI-NRS), Scalpdex, and Dermatology Life Quality Index (DLQI)/Children's DLQI
  - Safety and local tolerability were also assessed

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. [b]An 11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable) for the preceding 24 hours. [c]A 23-item questionnaire answered on a 5-point scale ranging from 1 (never) to 5 (all the time). [d]A 10-item questionnaire answered on 4-point scales (range: 0 (not at all/not relevant) to 3 (very much)).
BSA: body surface area; CDLQI: Children's Dermatology Life Quality Index; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; QD: once daily; SD, seborrheic dermatitis; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

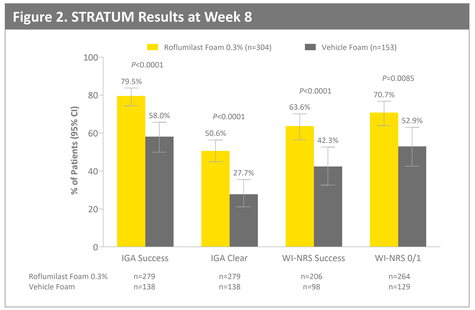
- Baseline patient demographics and disease characteristics were similar between the groups (Table 1)
- The mean duration since onset of seborrheic dermatitis diagnosis was 128 months (~10.7 years)

Table 1. Baseline Disease Characteristics

	Roflumilast Foam 0.3% (n=304)	Vehicle Foam (n=153)
Age, years, mean (SD)	43.2 (16.8)	41.8 (17.5)
Sex, n (%)		
Male	153 (50.3)	75 (49.0)
Female	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)
>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, 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 (SD)	5.06 (2.34)	4.74 (2.29)
WI-NRS ≥4, n (%)	206 (67.8)	98 (64.1)
BSA, %, mean (SD)	2.89 (2.03)	2.98 (2.57)
DLQI, mean (SD)	5.8 (4.4)	4.7 (6.2)
Scalpdex, mean (SD) total score	41.3 (19.8)	37.8 (20.2)
Duration since seborrheic dermatitis diagnosis, mean (SD)	137.9 (134.4)	108.5 (97.5)

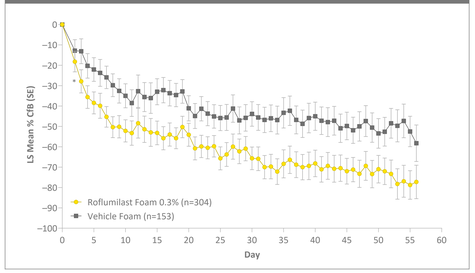
- Significantly more roflumilast-treated patients than vehicle-treated patients achieved the primary efficacy endpoint of IGA Success and IGA status of Clear at Week 8 (Figure 2)
  - Percentages of patients achieving IGA Success and IGA Clear were also greater with roflumilast at Weeks 2 and 4
- Among patients with baseline WI-NRS score ≥2, more roflumilast-treated than vehicle-treated patients achieved WI-NRS score 0/1 at Week 8 (70.7% vs 52.9%; P=0.0085; Figure 2), with improvements in itch compared with vehicle as early as 48 hours after first treatment (mean percent change from baseline [CfB]: −27.87% vs −13.11%; nominal P=0.0024; Figure 3)

Figure 2. STRATUM Results at Week 8



CI: confidence interval.

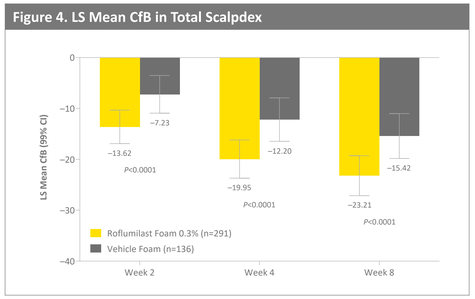
Figure 3. Daily LS Mean Percent CfB in WI-NRS



*P=0.0024 at 48 hours after dosing and P<0.05 for difference from vehicle for all time points assessed after.
Observed data, intent-to-treat population.
CfB: change from baseline; LS: least squares; SE: standard error.

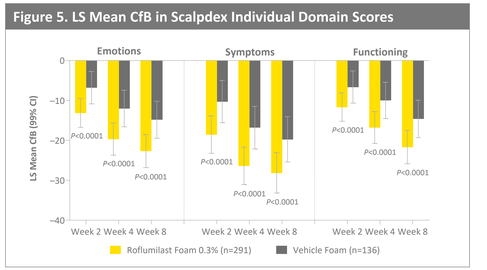
- Roflumilast-treated patients with scalp involvement had greater improvements in least squares (LS) mean CfB Scalpdex score at Week 8 (−23.21 vs −15.42; nominal P<0.001; Figures 4 and 5)

Figure 4. LS Mean CfB in Total Scalpdex



Analyses of Scalpdex are limited to patients in the analysis population who have SD involvement on the scalp.
CfB: change from baseline; CI: confidence interval; LS: least squares.

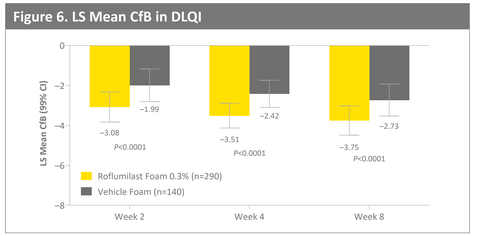
Figure 5. LS Mean CfB in Scalpdex Individual Domain Scores



Scalpdex: a 23-item questionnaire answered on a 5-point scale ranging from 1 (never) to 5 (all the time). Analyses of Scalpdex are limited to patients in the analysis population who have SD involvement on the scalp.
CfB: change from baseline; CI: confidence interval; LS: least squares; SD: seborrheic dermatitis.

- Roflumilast-treated patients reported greater improvements in LS mean CfB DLQI score (−3.8 vs −2.7; nominal P<0.001; Figure 6)

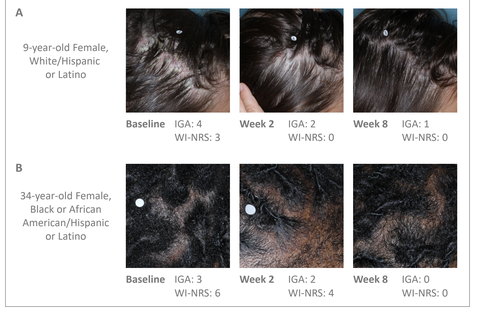
Figure 6. LS Mean CfB in DLQI



DLQI score is the sum of 10 questions rated concerning the patient's perception of the impact of skin disease on different aspects of their health-related quality of life over the last week. It ranges from 0 to 30, where higher scores indicate the most impact on the patient's health-related quality of life.
CfB: change from baseline; CI: confidence interval; LS: least squares.

- Once-daily treatment with roflumilast foam 0.3% for 8 weeks resulted in improvements in SD, as shown in a series of patient photos (Figure 7)

Figure 7. Improvement in SD in a Patient Treated With Roflumilast Foam 0.3% QD



- 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)
- At all time points, ≥98.9% of patients had no evidence of irritation on investigator-rated assessments and ≥92.4% of patients reported a score of 0 (no sensation) or 1 (slight warm, tingling sensation; not really bothersome) on patient-rated tolerability

Table 2. Adverse Events

n (%)	Roflumilast Foam 0.3% (n=304)	Vehicle Foam (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 an 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 include diarrhea/hematochezia/abdominal pain in 1 patient with a past history of Crohn's disease and decreased potassium in the second patient. [c]Presented in descending order for overall rates.
AE: adverse event; COVID-19: coronavirus disease 2019; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

CONCLUSION

- Treatment with once-daily roflumilast foam 0.3% provided a clinically meaningful reduction in pruritus and improvement in quality of life
- Local tolerability was favorable and all patients had low rates of discontinuation

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DISCLOSURES

- NB, FC-B, JD, LKF, LSG, IT, and MZ are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DK, PB, DRB, and DHC are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.