A Randomized, Double-blind, Vehicle-Controlled Phase 2a Study Evaluating Once Daily Roflumilast Foam 0.3% in Patients With Moderate to Severe Seborrheic Dermatitis

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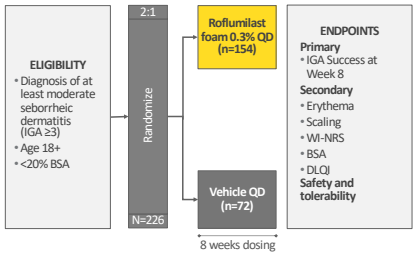
INTRODUCTION

- Seborrheic dermatitis (Seb Derm) is a chronic inflammatory skin condition that causes physical discomfort and emotional burden for patients[1,2]
  - Seb Derm is characterized by erythematous, scaly plaques, with a yellowish, oily, moist, and/or greasy appearance and affects areas with abundant sebaceous glands[3,4]
  - Seb Derm can negatively impact quality of life, particularly in patients with more severe disease[5]
- Topical treatments include antifungals, steroids, immunomodulators, and dandruff shampoos,[3,4] but efficacious and safe options are needed, especially for long-term use
- Roflumilast is a selective and highly potent phosphodiesterase-4 inhibitor being investigated for once-daily, nonsteroidal, treatment of several dermatologic conditions,[6] including Seb Derm
- A phase 2, 8-week study investigating roflumilast foam 0.3% once-daily for the treatment of Seb Derm (ClinicalTrials.gov identifier: NCT04091646) was recently completed

METHODS

- This was a phase 2a, parallel-group, double-blind, vehicle-controlled, 8-week clinical trial of once-daily roflumilast foam 0.3% for the treatment of Seb Derm
- Eligible patients were adults (≥18 years) with a clinical diagnosis of Seb Derm of at least 3 months' duration, an Investigator Global Assessment (IGA) score ≥3 (moderate severity), and affecting ≤20% of the body surface area (BSA), including the scalp, face, trunk, and/or intertriginous areas (**Figure 1**)
- Patients were randomized in a 2:1 ratio to roflumilast foam 0.3% or vehicle foam, which was applied once daily to lesions of Seb Derm
- The intention-to-treat (ITT) population included all randomized patients, while the modified intent-to-treat (mITT) population included all randomized patients with the exception of 2 patients who missed the Week 8 IGA assessment due to the COVID-19 disruption
  - The primary efficacy analysis was based on the mITT population and repeated for the ITT population
- The primary efficacy endpoint was analyzed using a Cochran-Mantel-Haenszel test stratified by study site and baseline disease severity; statistical significance was concluded at the 10% significance level (2-sided)
  - Missing IGA scores were imputed using multiple imputation

Figure 1. Study Design



IGA Success = *Clear* or *almost clear* plus ≥2-grade improvement from baseline. BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; QD: once daily; WI-NRS: Worst Itch-Numeric Rating Scale.

RESULTS

- A total of 226 patients were randomized to roflumilast foam (n=154) or vehicle foam (n=72; **Figure 2**)
  - One roflumilast-treated patient and one vehicle-treated patient withdrew or missed the Week 8 evaluation due to COVID-19 disruption (**Table 1**)
- Overall, 92% of patients completed the study (**Table 2**)
  - Few patients discontinued due to adverse events (AEs)
- Demographics and baseline characteristics were similar in the treatment groups (**Table 3**)

Table 1. Study Populations

Patients, n (%)	Roflumilast Foam 0.3%	Vehicle	Overall
ITT	154 (100)	72 (100)	226 (100)
Safety population	154 (100)	72 (100)	226 (100)
mITT*	153 (99.4)	71 (98.6)	224 (99.1)
PRU4	125 (81.2)	59 (81.9)	184 (81.4)

*Excludes 2 patients: One roflumilast-treated patient (31003) who was enrolled March 6, then withdrew consent due to the fear of contracting COVID-19 (informed site May 1), with no post-baseline visits, and 1 vehicle-treated patient (17006) who missed Week 8 IGA due to COVID, but did not discontinue due to COVID, and came back for the Week 9 visit. ITT: intent-to-treat, all randomized patients. Safety population: all patients who were enrolled and received at least 1 confirmed dose of investigational product. mITT: modified intent-to-treat, all randomized patients except those who missed the Week 8 an Investigator Global Assessment (IGA) assessment specifically due to COVID-19 disruption. PRU4 population: subset of ITT, includes patients with Worst Itch-Numeric Rating Scale pruritus score ≥4 at baseline.

Table 2. Patient Disposition

Patients, n (%)	Roflumilast Foam 0.3% (n=154)	Vehicle (n=72)	Overall (n=226)
Completed	141 (91.6)	67 (93.1)	208 (92.0)
Prematurely discontinued	13 (8.4)	5 (6.9)	18 (8.0)
Reason for discontinuation			
Withdrawal by patient	4 (2.6)	1 (1.4)	5 (2.2)
Protocol violation	0	1 (1.4)	1 (0.4)
Lost to follow-up	6 (3.9)	2 (2.8)	8 (3.5)
Adverse event	2 (1.3)	1 (1.4)	3 (1.3)
Other	1 (0.6)	0	1 (0.4)

Table 3. Demographics (Safety Population)

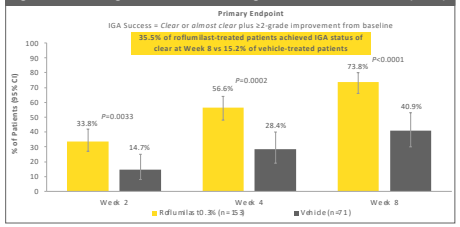
	Roflumilast Foam 0.3% (n=154)	Vehicle (n=72)	Overall (n=226)
Age in years, mean	45.3	44.2	44.9
Gender, n (%)			
Male	76 (49.4)	40 (55.6)	116 (51.3)
Female	78 (50.6)	32 (44.4)	110 (48.7)
Ethnicity, n (%)			
Hispanic or Latino	29 (18.8)	16 (22.2)	45 (19.9)
Not Hispanic or Latino	125 (81.2)	56 (77.8)	181 (80.1)
Race, n (%)			
American Indian or Alaskan Native	1 (0.6)	0	1 (0.4)
Asian	7 (4.5)	1 (1.4)	8 (3.5)
Black or African American	17 (11.0)	6 (8.3)	23 (10.2)
Native Hawaiian or other Pacific Islander	0	0	0
White	123 (79.9)	62 (86.1)	185 (81.9)
Other	1 (0.6)	2 (2.8)	3 (1.3)
More than one race	5 (3.2)	1 (1.4)	6 (2.7)
BSA, mean %	3.3	3.0	3.2
Baseline IGA (0–4), n (%)			
3 – Moderate	141 (91.6)	69 (95.8)	210 (92.9)
4 – Severe	13 (8.4)	3 (4.2)	16 (7.1)
Baseline erythema (0–3), n (%)			
2 – Moderate	135 (87.7)	66 (91.7)	201 (88.9)
3 – Severe	19 (12.3)	6 (8.3)	25 (11.1)
Baseline scaling (0–3), n (%)			
2 – Moderate	130 (84.4)	58 (80.6)	188 (83.2)
3 – Severe	24 (15.6)	14 (19.4)	38 (16.8)
WI-NRS			
Mean	5.8	5.7	5.8
Median	6.0	6.0	6.0
≥4, n (%)	125 (81.2)	59 (81.9)	184 (81.4)
Facial involvement, n (%)	100 (64.9)	36 (50.0)	136 (60.2)

Safety population: all patients who were enrolled and received at least 1 confirmed dose of investigational product. BSA: body surface area; IGA: Investigator Global Assessment; WI-NRS: Worst Itch-Numeric Rating Scale.

Efficacy

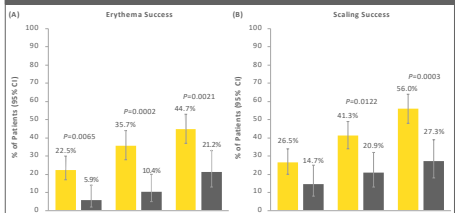
- Roflumilast foam 0.3% demonstrated significant and rapid improvement in Seb Derm as indicated by the percentage of patients achieving IGA Success (**Figure 2**)
  - A significant benefit was observed by Week 2 (the first timepoint evaluated)
- Roflumilast foam 0.3% significantly improved both redness (Erythema Success) and scaling (Scaling Success) associated with Seb Derm (**Figure 3**)
- Roflumilast foam 0.3% resulted in significant and rapid improvement in itch as indicated by improvements on the WI-NRS (**Figure 4**)
- Roflumilast foam 0.3% provided treatment benefit by reducing BSA affected and improving Dermatology Life Quality Index (DLQI; **Figure 5**)

Figure 2. Percentages of Patients Achieving IGA Success at Each Visit (mITT)



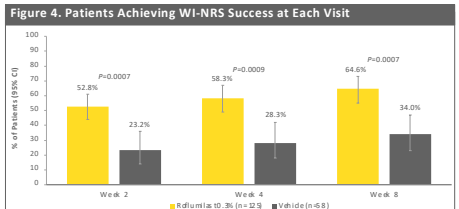
CI: confidence interval; IGA: Investigator Global Assessment; mITT: modified intent-to-treat, all randomized patients except those who missed the Week 8 IGA assessment specifically due to COVID-19 disruption.

Figure 3. Patients Achieving Erythema Success (A) and Scaling Success (B) at Each Visit (mITT)



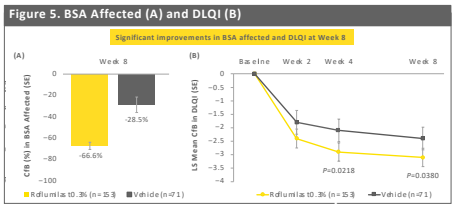
Erythema success defined as Erythema Score of none (0) or mild (1) plus ≥2-grade improvement from baseline; Scaling success defined as Scaling Score of none (0) or mild (1) plus ≥2-grade improvement from baseline. CI: confidence interval; mITT: modified intent-to-treat, all randomized patients except those who missed the Week 8 Investigator Global Assessment specifically due to COVID-19 disruption.

Figure 4. Patients Achieving WI-NRS Success at Each Visit



WI-NRS success defined as achievement of a ≥4-point improvement from baseline score of ≥4. CI: confidence interval; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 5. BSA Affected (A) and DLQI (B)



BSA: body surface area; CfB: change from baseline; DLQI: Dermatology Life Quality Index; LS: least square; SE: standard error.

Safety

- Rates of AEs were low (**Table 4**)
- Few treatment-related AEs were reported
- Very few AEs led to study discontinuation
  - Rates of discontinuation were similar between roflumilast and vehicle groups
- No patients had a serious AE
- ≥99% of roflumilast-treated and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator-rating of local tolerability

Table 4. Adverse Events

n (%)	Roflumilast Foam 0.3% (n=154)	Vehicle Foam (n=72)
Patients with any TEAE	37 (24.0)	13 (18.1)
Patients with any treatment-related TEAE	3 (1.9)	3 (4.2)
Patients with any serious AE	0	0
Patients who discontinued study due to AE[a]	2 (1.3)	2 (2.8)
Most common TEAE (>2% in any group), preferred term		
Contact dermatitis[b]	3 (1.9)	2 (2.8)
Insomnia	3 (1.9)	1 (1.4)
Nasopharyngitis	3 (1.9)	0

[a]AEs leading to discontinuation for roflumilast were application-site pain (1 patient), migraine, dyspnea (both reported in the same patient). In the vehicle group: application-site dysesthesia. [b]All cases of contact dermatitis were reported to be unrelated to treatment and did not require a change in dosing of study intervention; 2 cases were reported as poison ivy rash. Data are presented for safety population (all patients who were enrolled and received at least 1 confirmed dose of investigational product). AE: adverse event; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Roflumilast foam 0.3% demonstrated significant improvement in IGA Success, erythema, scaling, and itch
  - The improvements in IGA Success were statistically significant at the first post-baseline visit (Week 2) and continued through Week 8
  - Roflumilast foam resulted in significant improvements in itch by Week 2
    - ~80% of patients reported notable itch at baseline (WI-NRS ≥4)
  - Roflumilast reduced BSA affected and improved patient quality of life (DLQI)
- Rates of treatment-related AEs, discontinuations due to AEs, and application-site pain were low and similar to vehicle
- In this phase 2a study, investigational, once-daily roflumilast foam 0.3% was demonstrated to be a safe, well-tolerated, and effective treatment of Seb Derm with early onset of action and warrants further investigation as a potentially novel treatment

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DISCLOSURES

MZ, **JD**, **LK**, **AM**, **LSG**, **JA-L**, **MB**, **SB**, **KE**, **LIG**, **STG**, **LKF**, **SF**, **SEK**, **EL**, **CWL**, **DMP**, **DPT**, and **PSY** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **AF**, **RCH**, **PB**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.