Long-term Safety and Efficacy of Roflumilast Foam 0.3% in Patients With Seborrheic Dermatitis in a 24–52-week, Open-label Phase 2 Trial

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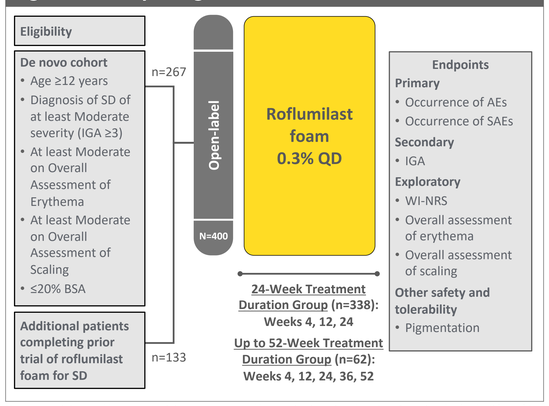
INTRODUCTION

- Seborrheic dermatitis (SD) is a chronic inflammatory skin condition characterized by a range of clinical features including erythematous, scaly patches and plaques in areas with abundant sebaceous glands (face, scalp, chest, back)[1,2]
  - It is often associated with pruritus, and in patients with skin of color, may be accompanied by dyspigmentation[1,2]
  - SD can have a negative impact on patient quality of life, especially among those with more severe SD[3]
- Chronic use of current topical treatment options, such as topical corticosteroids and off-label use of topical calcineurin inhibitors, is limited due to risk of local skin and other side effects[4]
- Roflumilast is a selective and highly potent phosphodiesterase 4 (PDE4) inhibitor with greater affinity for PDE4 than apremilast or crisaborole and approximately 25- to >300-fold more potent based on in vitro assays[5]
  - Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for long-term management of various dermatologic conditions, including chronic plaque psoriasis (approved July 29, 2022 by the US Food and Drug Administration), atopic dermatitis, and SD
- Efficacy, safety, and tolerability of roflumilast foam in psoriasis have been demonstrated in a phase 2a trial in patients with SD[6]
- Here, we report the results of a phase 2, open-label safety trial (NCT04445987) of roflumilast foam 0.3% for 24–52 weeks conducted in patients (aged ≥12 years) with SD

METHODS

- This phase 2, open-label safety trial was conducted in patients (aged ≥12 years) with at least moderate SD who successfully completed a prior roflumilast foam trial (n=133) and in patients naïve to roflumilast and its vehicle (n=267; **Figure 1** and **Table 1**)
- Patients applied roflumilast foam 0.3% once daily to all active SD lesions, including any new lesions that developed during the trial, unless otherwise instructed by the Investigator, for up to 52 weeks
  - All affected body locations could be treated, including the scalp, face, trunk, and intertriginous areas
- The primary endpoint was safety; efficacy was also assessed

Figure 1. Study Design



Hypopigmentation and hyperpigmentation were assessed by investigators at each visit on 4-point scales (scale: 0 [none] to 3 [severe]).
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.

RESULTS

Table 1. Baseline Demographics and Disease Characteristics[a]

n (%)	Roflumilast Foam 0.3% (n=400)
Age in years, mean (Std Dev)	43.3 (16.4)
Sex	
Male, n (%)	197 (49.3)
Female, n (%)	203 (50.8)
Ethnicity[b]	
Hispanic or Latino	115 (28.8)
Not Hispanic or Latino	283 (70.8)
Race, n (%)	
American Indian or Alaska Native	0
Asian	17 (4.3)
Black or African American	51 (12.8)
Native Hawaiian or Other Pacific Islander	1 (0.3)
White	319 (79.8)
Other	6 (1.5)
More than 1 race	3 (0.8)
Not reported/missing	3 (0.8)
Seborrheic dermatitis-affected BSA, mean % (Std Dev)	3.6 (3.1)
IGA score, n (%)	
3 (moderate)	341 (85.3)
4 (severe)	44 (11.0)
Erythema score, n (%)	
3 (moderate)	339 (84.8)
4 (severe)	45 (11.3)
Scaling score, n (%)	
3 (moderate)	314 (78.5)
4 (severe)	69 (17.3)
Scalpdex Total Score, mean (Std Dev)	39.5 (20.1)
WI-NRS, mean score (Std Dev)	5.7 (2.6)
WI-NRS score ≥4, n (%)	316 (75.7)

[a]Baseline was the last observation recorded before the first dose of roflumilast foam 0.3% recorded on Day 1 of parent trial (patients treated with roflumilast in parent trial) or this trial (patients treated with vehicle in parent trial or de novo patients). [b]Ethnicity missing for 2 patients.
BSA: body surface area; IGA: Investigator Global Assessment; Std Dev: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Safety

- Roflumilast foam 0.3% was well tolerated with low rates of adverse events (AEs) **(Table 2)**
  - Overall, 81.8% of patients completed the trial
  - Five (1.3%) patients discontinued due to an AE
- 130 (32.5%) patients experienced a treatment-emergent AE
  - Most AEs were mild or moderate in severity
  - 22 (5.5%) patients had an AE that was considered treatment-related
  - Seven (1.8%) patients experienced a serious AE, none of which were treatment-related
- Investigator-rated local tolerability assessments demonstrated ≥96.0% of patients had no evidence of irritation at each visit
- For patient-rated local tolerability, ≥95.2% of patients reported no or mild sensation at each visit

Pigmentation

- Most patients with hyper- or hypopigmentation at baseline experienced full resolution by Week 24 (n=278)
  - Of the 29 (10.4%) patients who had hypopigmentation at baseline, 20/29 (69.0%) experienced full resolution
  - Of the 24 (8.6%) patients who had hyperpigmentation at baseline, 17/24 (70.8%) experienced full resolution
- Of the patients who remained in the study through 52 weeks (n=46)
  - 11 (23.9%) patients had hypopigmentation at baseline and 8/11 (72.7%) experienced full resolution
  - 7 (15.2%) patients had hyperpigmentation at baseline and 6/7 (85.7%) experienced full resolution
- At Week 24, new instances of hypopigmentation (n=1) and hyperpigmentation (n=5) were uncommon

Table 2. Adverse Events

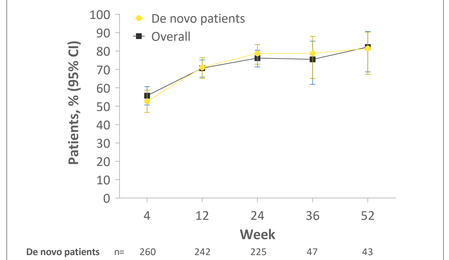
n (%)	Roflumilast Foam 0.3% (n=400)
Patients with any TEAE	130 (32.5)
Patients with any treatment-related TEAE	22 (5.5)
Patients with any SAE	7 (1.8)
Patients with treatment-related SAE	0
Patients who discontinued trial due to AE	5 (1.3)
Most common TEAE (≥1%), preferred term	
COVID-19	15 (3.8)
Headache	13 (3.3)
Urinary tract infection	7 (1.8)
Application-site pain	6 (1.5)
Alanine aminotransferase increased	6 (1.5)
Nausea	5 (1.3)
Back pain	5 (1.3)
Diarrhea	4 (1.0)
Weight decreased	4 (1.0)
Depression	4 (1.0)
Insomnia	4 (1.0)

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

Efficacy

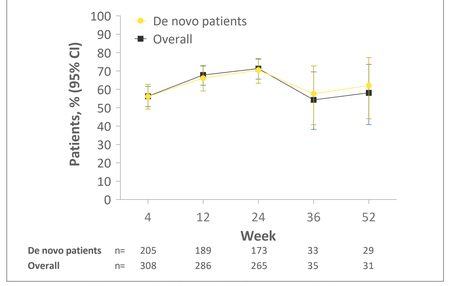
- Once-daily treatment with roflumilast foam 0.3% resulted in durable improvement on the Investigator Global Assessment (IGA)
- Over half (55.7%) of patients achieved an IGA status of Clear or Almost Clear at the first follow-up visit at Week 4, and over three-quarters (76.2%) of patients achieved IGA of Clear or Almost Clear at Week 24 **(Figure 2)**
  - In patients treated for 52 weeks (n=62), 82.2% of patients achieved IGA status of Clear or Almost Clear at Week 52
  - Rates of achievement of IGA status of Completely Clear were 43.1% and 53.3% at Weeks 24 and 52, respectively
  - Of the 345 patients who entered the long-term trial with or achieved IGA of Clear or Almost Clear during the trial, the Kaplan-Meier median duration patients maintained this response was 44.0 weeks (~11 months)
- Treatment with roflumilast foam 0.3% resulted in sustained improvement in itch with 71.3% of patients achieving ≥4-point improvement on the WI-NRS from baseline at Week 24 (n=265) and 58.1% at Week 52 (n=31; **Figure 3**)
- Roflumilast treatment also resulted in high level of patients with Erythema and Scaling scores of 0 (none) that lasted for up to 52 weeks **(Figures 4** and **5)**

Figure 2. Percentage of Patients With IGA Clear or Almost Clear



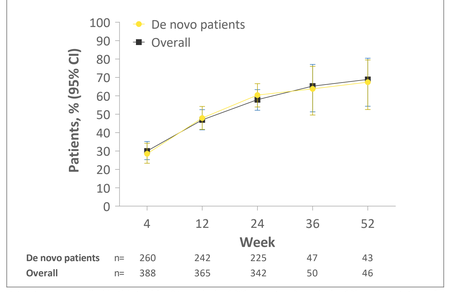
Patients were enrolled in this trial for 24 weeks (n=338) or up to 52 weeks (n=62); no imputation of missing values. De novo: patients naïve to roflumilast and its vehicle.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Percentage of Patients With WI-NRS Success



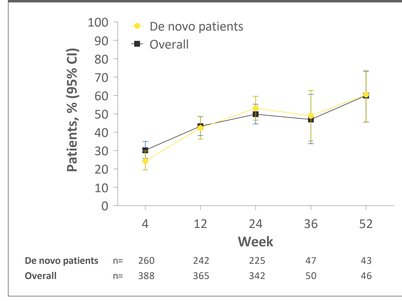
Patients were enrolled in this trial for 24 weeks (n=338) or up to 52 weeks (n=62); no imputation of missing values. De novo: patients naïve to roflumilast and its vehicle.
WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4.
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 4. Percentage of Patients With Erythema Score of 0 (No Erythema)



Patients were enrolled in this trial for 24 weeks (n=338) or up to 52 weeks (n=62); no imputation of missing values. De novo: patients naïve to roflumilast and its vehicle.
Scale for Overall Assessment of Erythema: 0 = none, 1 = mild, 2 = moderate, 3 = severe.
CI: confidence interval.

Figure 5. Percentage of Patients With Scaling Score of 0 (No Scaling)



Patients were enrolled in this trial for 24 weeks (n=338) or up to 52 weeks (n=62); no imputation of missing values. De novo: patients naïve to roflumilast and its vehicle.
Scale for Overall Assessment of Scaling: 0 = none, 1 = mild, 2 = moderate, 3 = severe.
CI: confidence interval.

CONCLUSIONS

- In this long-term safety trial, roflumilast foam 0.3% demonstrated favorable safety and tolerability and effectively maintained improvements in IGA and WI-NRS in patients with SD
- The local tolerability profile as assessed by both patients and investigators was favorable and consistent with the phase 2a study
- Most patients with hypo- or hyperpigmentation experienced full resolution
- Once-daily treatment with roflumilast foam 0.3% resulted in durable improvement on efficacy endpoints
- These data support further investigation of roflumilast foam 0.3% as a nonsteroidal, once-daily topical treatment option for SD with a mechanism of action that supports acute and chronic use across affected areas, including the face and scalp

REFERENCES

1. Dessinioti C, Katsambas A. *Clin Dermatol* 2013;31:343–351.
2. Adalsteinsson JA, et al. *Exp Dermatol* 2020;29:481–489.
3. Peyrí J, et al. *Actas Dermosifiliogr* 2007;98:476–482.
4. Wollenberg A, et al. *J Eur Acad Dermatol Venereol* 2020;34:2717–2744.
5. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
6. Zirwas M, et al. 30th Congress of the European Academy of Dermatology and Venereology (EADV) Virtual, September 29-October 2, 2021.

DISCLOSURES

AFA, **MZ**, **MB**, **ZDD**, **JD**, **AYM**, **EL**, **LKF**, and **FEC-B** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **BB**, **SK**, **SS**, **DHC**, **PB**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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