Effect of Roflumilast Foam 0.3% Treatment of Seborrheic Dermatitis on Patient Quality of Life: Results From a Phase 2 Study

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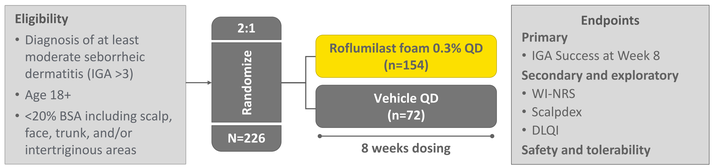
INTRODUCTION

- Seborrheic dermatitis (Seb Derm) is a chronic inflammatory skin condition characterized by erythematous, scaly plaques, with a yellowish, oily, moist, and/or greasy appearance, which causes physical discomfort and emotional burden for patients[1,2]
- About 95% of patients with Seb Derm have scalp involvement, which can be painful and itchy, negatively impacting quality of life, particularly in patients with more severe disease[3,4]
- Scalpdex is a validated, scalp dermatitis-specific instrument in which patients score 23 questions across 3 quality-of-life domains including symptoms, emotion, and function[3]
- Roflumilast is a selective and highly potent phosphodiesterase-4 (PDE-4) inhibitor with greater affinity for PDE-4 than apremilast or crisaborole and is 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 various dermatologic conditions, including psoriasis, atopic dermatitis, seborrheic dermatitis, and scalp psoriasis
  - The results of a phase 2a, randomized clinical trial are presented, with focus on the impact of roflumilast foam 0.3% on quality of life using Dermatology Life Quality Index (DLQI) and Scalpdex (ClinicalTrials.gov identifier: NCT04091646)

METHODS

- This was a phase 2a, parallel-group, double-blind, vehicle-controlled clinical trial in 226 adult (aged ≥18 years) patients with a clinical diagnosis of Seb Derm (**Figure 1**)
- Patients were randomized to once-daily roflumilast foam 0.3% (n=154) or vehicle foam (n=72) for 8 weeks
- The primary endpoint was Investigator Global Assessment (IGA) Success, defined as achievement of an IGA score of Clear or Almost Clear plus 2-grade improvement from baseline at Week 8

Figure 1. Study Design



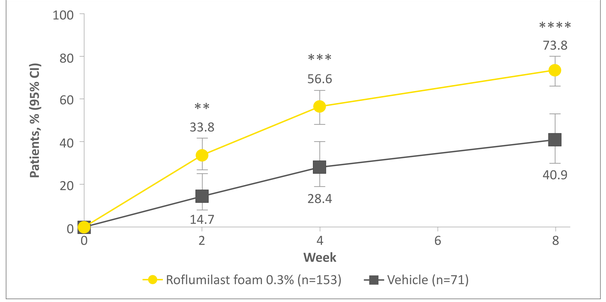
ClinicalTrials.gov identifier: NCT04091646

IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
The intent-to-treat (ITT) population included all randomized patients, whereas 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.
BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

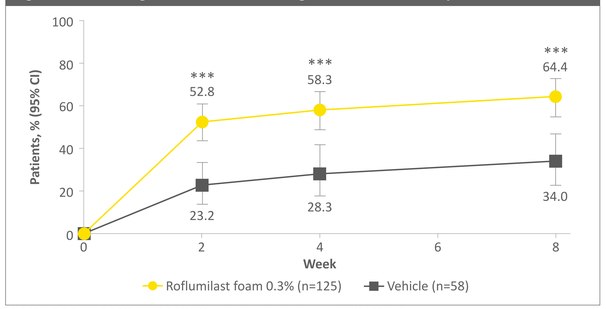
- Patients treated with roflumilast showed significant and rapid improvement across multiple endpoints including IGA Success, itching, and on the DLQI
  - Patients treated with roflumilast had rapid improvement on IGA Success and Worst Itch Numeric Rating Scale (WI-NRS) with significant differences occurring by Week 2, the first timepoint evaluated
  - 35.5% of roflumilast-treated patients achieved IGA status of Clear at Week 8 versus 15.2% of vehicle-treated patients (**Figure 2**)
  - About 65% of patients with a baseline WI-NRS ≥4 score achieved a 4-point response at Week 8 (**Figure 3**)
  - Patients treated with roflumilast had a significantly greater change from baseline (improvement) on the DLQI at Weeks 4 and 8 (**Figure 4**)
- Roflumilast improved health-related quality of life as indicated by significant reductions on all domain scores of the Scalpdex (**Figure 5**)
- Roflumilast foam 0.3% was well tolerated (**Table 1**)
  - ≥99% of roflumilast-treated and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator-rating of local tolerability

Figure 2. Percentage of Patients Achieving IGA Success



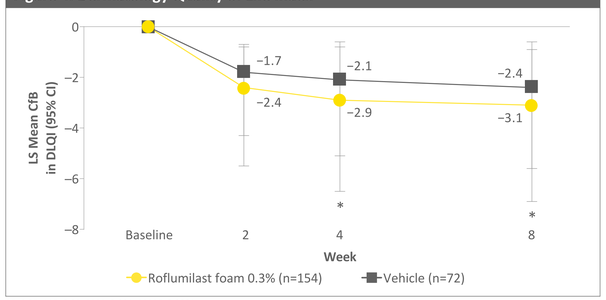
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Percentage of Patients Achieving WI-NRS 4-Point Response[a]



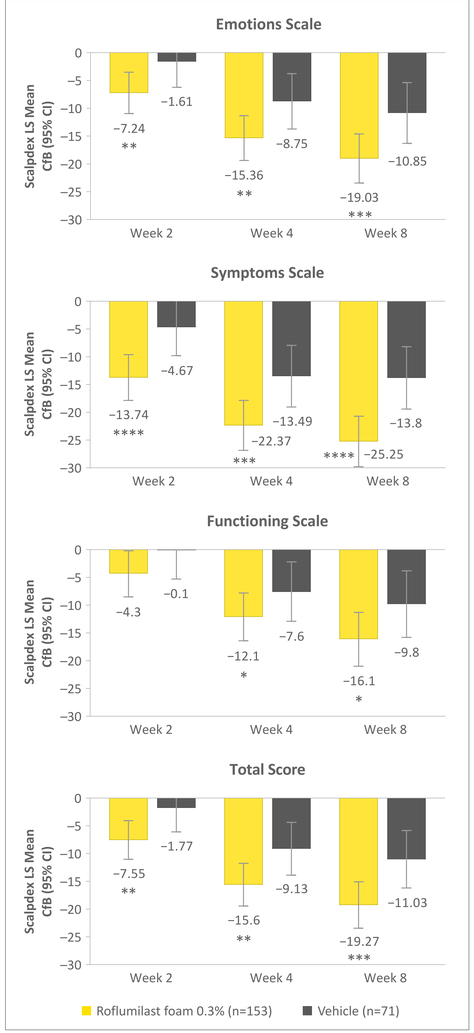
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Evaluated in patients with a baseline WI-NRS of ≥4
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 4. Dermatology Quality of Life Index



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
Cfb: change from baseline; CI: confidence interval; DLQI: Dermatology Life Quality Index; LS: least squares.

Figure 5. Scalpdex Domain Scores



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
Cfb: change from baseline; CI: confidence interval; LS: least squares.

Table 1. 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)	0 (0)
Patients who discontinued study due to AE[a]	2 (1.3)	1 (1.4)
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 (0)

[a]AEs leading to discontinuation for roflumilast were application-site pain (1 patient), migraine, and 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.
AE: adverse event; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Roflumilast foam 0.3% demonstrated significant improvement in IGA Success, itch, and health-related quality of life
  - The improvements in IGA Success were statistically significant at the first post-baseline visit (Week 2) and continued through Week 8
  - ~80% of patients reported notable itch at baseline (WI-NRS ≥4) and roflumilast foam 0.3% resulted in significant improvements in itch as early as Week 2 (the first timepoint measured)
  - Patients treated with roflumilast foam 0.3% reported improved quality of life versus vehicle across all symptom, emotional, and functional domains
- Rates of treatment-related AEs, discontinuations due to AEs, and application-site pain were low and similar to those of vehicle
- In this phase 2a study, treatment with once-daily roflumilast foam 0.3% resulted in improvements in disease severity and patient quality of life

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DISCLOSURES

ZDD, SF, LIG, TMJ, SEK, CWL, and **MZ** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **RCH, AF, PB,** and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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