Once-Daily Roflumilast Foam 0.3% Improves Severity and Burden of Itch in Patients With Scalp and Body Psoriasis in a Randomized, Double-blind, Vehicle-Controlled Phase 2b Study

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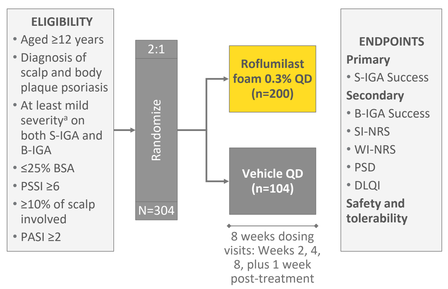
INTRODUCTION

- In patients with psoriasis, about 80% have scalp psoriasis[1]
  - Scalp psoriasis is often associated with itch, the most burdensome symptom of psoriasis[2]
  - Itching, flaking, and plaque visibility on the scalp can cause social embarrassment and adversely impact quality of life[3]
  - Treatment of scalp psoriasis is difficult because the hair may limit efficacy of creams and ointments and reduce treatment adherence[4]
- Roflumilast is a selective and highly potent phosphodiesterase-4 inhibitor being investigated as a once-daily, nonsteroidal, topical treatment for various dermatologic conditions
  - Roflumilast foam is uniquely formulated as an emollient, water-based, moisturizing foam that can be used on the scalp or body
  - Roflumilast cream met the primary and secondary endpoints and was well-tolerated in a phase 2b, randomized, double-blind, vehicle-controlled trial in adults with psoriasis[5]
- We investigated roflumilast foam for scalp and body psoriasis in a phase 2b, randomized, double-blind, vehicle-controlled 8-week study (ClinicalTrials.gov Identifier: NCT04128007)

METHODS

- This was a parallel-group, double-blind, vehicle-controlled clinical trial (Figure 1)
- Eligible patients were adults and adolescents ≥12 years old with diagnoses of scalp and body psoriasis for at least 6 months
- Patients were randomized 2:1 to roflumilast 0.3% or matching vehicle foam
- The primary efficacy endpoint was scalp-Investigator Global Assessment (S-IGA) Success, defined as achievement of an S-IGA score of *clear* or *almost clear* plus a 2-grade improvement from baseline at Week 8
- Efficacy endpoints were analyzed using a Cochran-Mantel-Haenszel test stratified by country, baseline S-IGA, and baseline body-IGA (B-IGA) category using multiple imputation for missing data
  - Statistical tests were conducted at the 5% significance level using 2-tailed tests

Figure 1. Study Design



• 96% power at α=0.05 to detect 22.4% difference between groups for S-IGA Success, based on 201 results showing 32.2% vs 9.8% IGA Success at Week 8[5]

[a]Protocol amendment 2: S-IGA entry criterion changed from ≥2 (mild) to ≥3 (moderate). S-IGA/B-IGA Success: IGA status of *clear* or *almost clear* plus ≥2-grade improvement from baseline. B-IGA: Body-Investigator Global Assessment; BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; NRS: Numeric Rating Scale; PASI: Psoriasis Area Severity Index; PSD: Psoriasis Symptom Diary; PSSI: Psoriasis Scalp Severity Index; QD: once daily; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

RESULTS

- A total of 304 patients were randomized to roflumilast foam 0.3% (n=200) or vehicle foam (n=104; intent-to-treat [ITT] population; Table 1)
  - Of these, 198 patients in the roflumilast group (99%) and 104 in the vehicle group (100%) received ≥1 confirmed dose of their study intervention (safety population)
- Most patients (83.7% to 88.5%) completed the study (Table 1)
- Baseline disease characteristics were balanced across treatment groups (Table 2)

Table 1. Patient Disposition

n (%)	Roflumilast 0.3% (n=200)	Vehicle (n=104)
Completed	177 (88.5)	87 (83.7)
Prematurely discontinued	23 (11.5)	17 (16.3)
Reason for discontinuation		
Withdrawal by subject	9 (4.5)	6 (5.8)
Noncompliance	1 (0.5)	0
Protocol violation	0	0
Lost to follow-up	8 (4.0)	7 (6.7)
Adverse event	5 (2.5)	2 (1.9)
Other	0	2 (1.9)

- Rates of discontinuation due to adverse event (AE) were low

Table 2. Baseline Disease Characteristics (ITT Population)

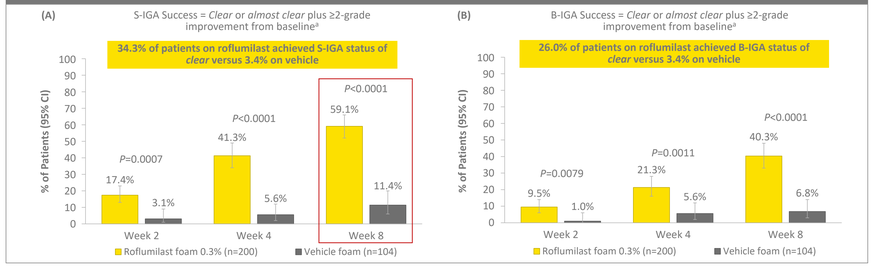
n (%)	Roflumilast Foam 0.3% (n=200)[a]	Vehicle Foam (n=104)
BSA, mean %	8.0	7.6
Baseline S-IGA		
2 – Mild	18 (9.0)	14 (13.5)
3 – Moderate	151 (75.5)	80 (76.9)
4 – Severe	29 (14.5)	10 (9.6)
Baseline B-IGA		
2 – Mild	69 (34.5)	39 (37.5)
3 – Moderate	119 (59.5)	60 (57.7)
4 – Severe	10 (5.0)	5 (4.8)
PSSI, mean (SD)	22.4 (12.5)	20.9 (11.7)
PASI, mean (SD)	7.2 (4.3)	6.8 (4.4)
SI-NRS, mean (SD)	6.4 (2.4)	6.6 (2.3)
SI-NRS, ≥4, n (%)	173 (86.5)	96 (92.3)
WI-NRS, mean (SD)	6.4 (2.48)	6.7 (2.32)
WI-NRS ≥4, n (%)	165 (82.5)	94 (90.4)
PSD total score mean (SD)	78.5 (39.92)	84.3 (38.76)
PSD Item 1: severity of itch, mean (SD)	6.3 (2.54)	6.7 (2.07)
PSD Item 2: burden of itch, mean (SD)	6.1 (2.73)	6.5 (2.50)
DLQI, mean (SD)	6.6 (5.18)	6.8 (4.66)

[a]Two patients were missing baseline values due to capture outside of the date-time visit window and were not evaluable. B-IGA: Body-Investigator Global Assessment; BSA: body surface area; DLQI: Dermatology Life Quality Index; ITT: intent-to-treat; PASI: Psoriasis Area Severity Index; PSD: Psoriasis Symptom Diary; PSSI: Psoriasis Scalp Severity Index; SD: standard deviation; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Efficacy

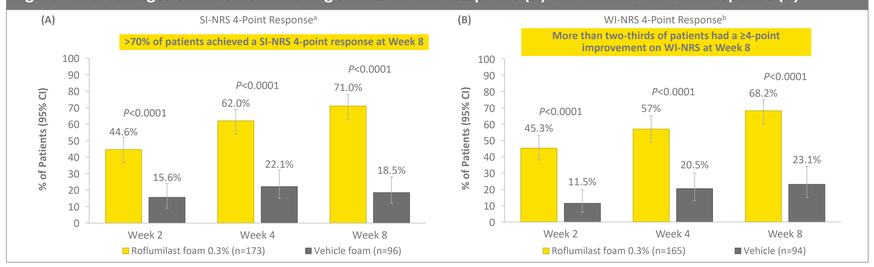
- Roflumilast foam significantly improved scalp and body psoriasis at all timepoints (Figure 2)
- Roflumilast significantly improved scalp and body itch by Week 2 and consistently improved itch through Week 8 (Figure 3)
- Roflumilast foam significantly improved patient-reported severity and burden of itch as indicated by improvements on the Psoriasis Symptom Diary (PSD) Items 1 (Severity of Itch) and 2 (Burden of Itch; Figure 4)
- Roflumilast-treated patients also had a significant improvement in quality of life as indicated by the Dermatology Life Quality Index (DLQI; Figure 5)

Figure 2. Percentages of Patients Achieving S-IGA Success (A) and B-IGA Success (B)



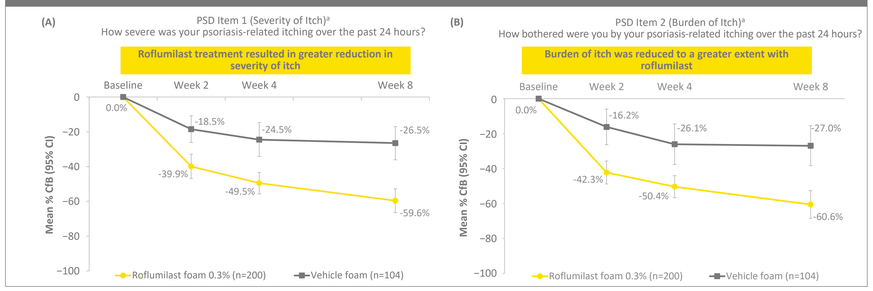
[a]Intent-to-treat population. B-IGA: Body-Investigator Global Assessment; CI: confidence interval; S-IGA: Scalp-Investigator Global Assessment.

Figure 3. Percentages of Patients Achieving SI-NRS 4-Point Response (A) and WI-NRS 4-Point Response (B)



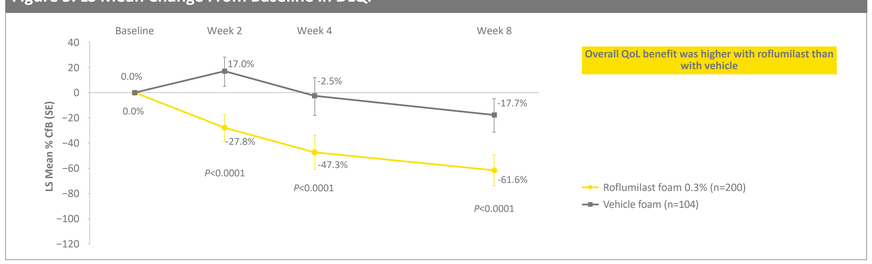
To control for multiple comparisons among the secondary endpoints, a multiplicity procedure was used. Upon successful testing of the primary endpoint, the α was partitioned to test secondary endpoints. [a]Evaluated in patients with SI-NRS Score ≥4 at baseline; [b]evaluated in patients with WI-NRS score ≥4 at baseline. CI: confidence interval; SI-NRS: Scalp Itch-Numeric Rating Scale; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 4. PSD Item 1 (Severity of Itch; A) and Item 2 (Burden of Itch; B)



To control for multiple comparisons among the secondary endpoints, a multiplicity procedure was used. Upon successful testing of the primary endpoint, the α was partitioned to test secondary endpoints. Estimates from an ANCOVA model with country, treatment, baseline S-IGA score category, baseline B-IGA score category, and baseline PSD score as independent variables. Intent-to-treat population. ANCOVA: analysis of covariance; B-IGA: Body-Investigator Global Assessment; CfB: change from baseline; CI: confidence interval; PSD: Psoriasis Symptom Diary; SE: standard error; S-IGA: Scalp-Investigator Global Assessment.

Figure 5. LS Mean Change From Baseline in DLQI



Estimates from an ANCOVA model with country, treatment, baseline S-IGA score category, baseline B-IGA score category, and baseline DLQI score as independent variables. Intent-to-treat population. ANCOVA: analysis of covariance; B-IGA: Body-Investigator Global Assessment; CfB: change from baseline; DLQI: Dermatology Life Quality Index; LS: least squares; QoL: quality of life; SE: standard error; S-IGA: Scalp-Investigator Global Assessment.

Safety

- Rates of treatment-emergent AEs and discontinuation due to AEs were low (Table 3)
- Treatment-related AEs were uncommon
- Only 1 patient had a serious AE (unrelated)
- Very few AEs led to study discontinuation
  - Discontinuation rates were similar between groups
- ≥99% of roflumilast- and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator rating of local tolerability

Table 3. Adverse Events

TEAEs, n (%)	Roflumilast Foam 0.3% (n=198)	Vehicle Foam (n=104)
Patients with any TEAE	46 (23.2)	20 (19.2)
Patients with any treatment-related TEAE	8 (4.0)	9 (8.7)
Patients with any serious AE[a]	1 (0.5)	0
Patients who discontinued study due to AE[b]	5 (2.5)	2 (1.9)
Most common TEAE (>1.5% in any group), preferred term		
Application-site pain	2 (1.0)	4 (3.8)
COVID-19	3 (1.5)	2 (1.9)
Psoriasis	1 (0.5)	2 (1.9)
Sinusitis	1 (0.5)	2 (1.9)
Hypertension	3 (1.5)	1 (1.0)
Diarrhea	3 (1.5)	0

[a]Serious AE: testicular torsion, unrelated. [b]AE leading to discontinuation: roflumilast: application-site pruritus, abdominal discomfort, diarrhea, headache, application-site pain, application-site discoloration, application-site irritation, lethargy; vehicle arm: psoriasis, application-site dermatitis. AE: adverse event; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Patients with scalp psoriasis need topical treatments that provide effective control of psoriasis with low incidence of side effects
- In this phase 2b study, once-daily roflumilast foam significantly improved both scalp and body psoriasis, apparent as early as 2 weeks after treatment initiation
  - Scalp and body itch abated by week 2 with further reduction throughout the study
- Roflumilast foam was well-tolerated with low rates of treatment-emergent AEs, application-site AEs, and discontinuations due to AE
  - Rates of these events were similar to vehicle
- Favorable safety profile and encouraging efficacy results warrant further investigation of once-daily roflumilast foam as a potential novel therapy for the treatment of scalp and body psoriasis

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DISCLOSURES

AYM, **JA-L**, **NB**, **MB**, **ARD**, **ZDD**, **MJG**, **SEK**, **LHK**, **KAP**, **DMP**, **MS**, **RS**, and **MZ** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/ or honoraria; **AF**, **PB**, **RCH**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.