Efficacy and Safety by Race and Ethnicity in a Randomized, Double-blind, Vehicle-Controlled, Phase 2a Study Evaluating Once-Daily Roflumilast Foam 0.3% in Patients With Seborrheic Dermatitis

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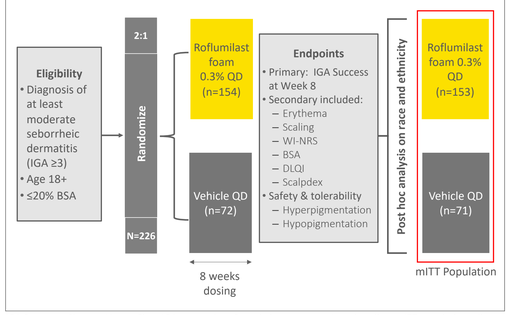
INTRODUCTION

- Seborrheic dermatitis (SD) is a chronic inflammatory skin condition characterized by erythematous, scaly plaques with a yellowish, oily, moist, and/or greasy appearance and affects areas with many sebaceous glands[1,2]
  - SD can negatively impact quality of life, particularly in patients with more severe disease[3]
  - Racial/ethnic variations in the prevalence, clinical presentation, and treatment of SD have been reported[4]
- Topical treatments include antifungals, steroids, immunomodulators, and anti-dandruff shampoos,[1,2] but efficacious and safe options are needed, especially for long-term use
- Topical roflumilast is a potent, phosphodiesterase 4 inhibitor being investigated for once-daily, nonsteroidal, treatment of several dermatologic conditions including SD, atopic dermatitis, and psoriasis (approved July 29, 2022 by the US Food and Drug Administration)[5,6]
- Here, we present the results of post hoc analyses by self-reported race and ethnicity from a phase 2 trial of roflumilast foam 0.3% in patients with moderate or severe SD (NCT04091646)

METHODS

- This was a phase 2a, parallel-group, double-blind, vehicle-controlled clinical trial of once-daily roflumilast foam 0.3% for treatment of SD
- Eligible patients were adults (≥18 years) with clinical diagnosis of SD of ≥3 months' duration, Investigator Global Assessment (IGA) score ≥3 (at least moderate severity), and affecting ≤20% of the body surface area, 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, which was applied once daily to SD lesions
- The primary efficacy endpoint was IGA Success (Clear/Almost Clear [score 0–1] plus ≥2-grade improvement) at Week 8
- Secondary endpoints included Erythema Success (score 0–1 plus ≥2-grade improvement), Scaling Success (score 0–1 plus ≥2-grade improvement), percentage of patients with baseline Worst Itch Numeric Rating Scale (WI-NRS) ≥4 achieving WI-NRS Success (≥4-point improvement), least squares mean change from baseline in Dermatology Life Quality Index (DLQI), and Scalpdex
- Hypopigmentation and hyperpigmentation were assessed by investigators on 4-point scales (0=none to 3=severe) at each visit
- Post hoc analyses were based on race and ethnicity

Figure 1. Study Design



IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline; mITT population: all randomized patients except 2 patients who missed the Week 8 IGA assessment due to COVID-19 disruption. BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; mITT: modified intent-to-treat; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

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

Table 1. Patient Disposition

n (%)	Roflumilast Foam 0.3% (n=154)	Vehicle (n=72)
Completed	141 (91.6)	67 (93.1)
Prematurely discontinued	13 (8.4)	5 (6.9)
Reason for discontinuation		
Withdrawal by patient	4 (2.6)	1 (1.4)
Protocol violation	0	1 (1.4)
Lost to follow-up	6 (3.9)	2 (2.8)
Adverse event	2 (1.3)	1 (1.4)
Other	1 (0.6)	0

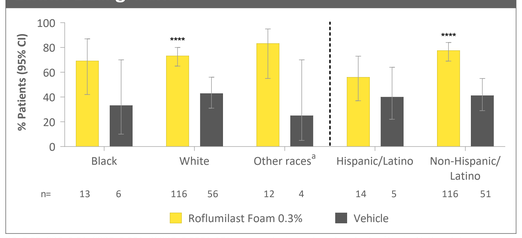
Table 2. Baseline Demographics and Disease Characteristics for the Overall ITT Population

n (%)	Roflumilast Foam 0.3% (n=154)	Vehicle (n=72)
Age in years, mean (Std Dev)	45.3 (17.0)	44.2 (16.3)
Sex, n (%)		
Male	76 (49.4)	40 (55.6)
Female	78 (50.6)	32 (44.4)
Ethnicity, n (%)		
Hispanic or Latino	29 (18.8)	16 (22.2)
Not Hispanic or Latino	125 (81.2)	56 (77.8)
Race, n (%)		
American Indian or Alaska Native	1 (0.6)	0
Asian	7 (4.5)	1 (1.4)
Black or African American	17 (11.0)	6 (8.3)
Native Hawaiian or Other Pacific Islander	0	0
White	123 (79.9)	62 (86.1)
Other	6 (3.8)	3 (4.2)
BSA, mean % (Std Dev)	3.3 (2.51)	3.1 (2.11)
Baseline IGA (0–4), n (%)		
3 (moderate)	141 (91.6)	69 (95.8)
4 (severe)	13 (8.4)	3 (4.2)
Baseline erythema (0–3), n (%)		
2 (moderate)	135 (87.7)	66 (91.7)
3 (severe)	19 (12.3)	6 (8.3)
Baseline scaling (0–3), n (%)		
2 (moderate)	130 (84.4)	58 (80.6)
3 (severe)	24 (15.6)	14 (19.4)
WI-NRS		
Mean score (Std Dev)	5.8 (2.66)	5.7 (2.33)
≥4, n (%)	125 (81.2)	59 (81.9)
Facial involvement, n (%)	100 (64.9)	36 (50.0)

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; ITT: intent-to-treat; Std Dev: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

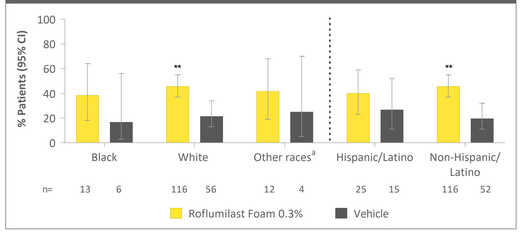
- Roflumilast foam 0.3% provided significant improvement in SD, as indicated by the percentage of patients achieving IGA Success at the first post-baseline visit (Week 2) and continued through Week 8 (data not shown)
  - Post hoc analyses indicated roflumilast efficacy versus vehicle for IGA Success demonstrated improvement regardless of race/ethnicity (Figure 2)
- Differences favoring roflumilast versus vehicle were observed for all secondary endpoints including Erythema, Scaling, WI-NRS Success, DLQI, and Scalpdex at Week 8
  - Secondary endpoints were consistent when analyzed by race or ethnicity (Figures 3–7)

Figure 2. IGA Success at Week 8 by Patient Racial and Ethnic Background



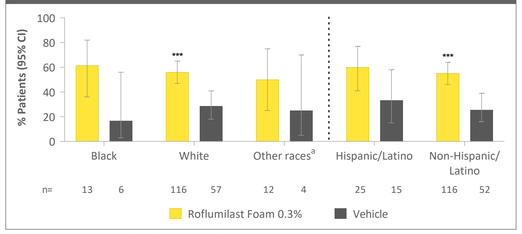
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
IGA success defined as IGA score of Clear or Almost Clear plus a ≥2-grade improvement from baseline.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Erythema Success at Week 8 by Patient Racial and Ethnic Background



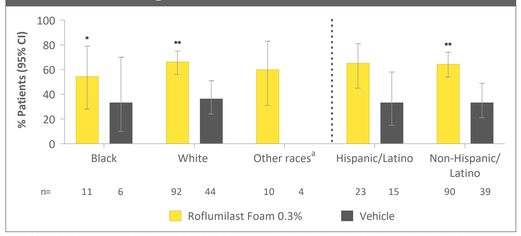
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
Erythema success defined as Erythema score 0 (None) or 1 (Mild) plus a ≥2-grade improvement from baseline.
CI: confidence interval.

Figure 4. Scaling Success at Week 8 by Patient Racial and Ethnic Background



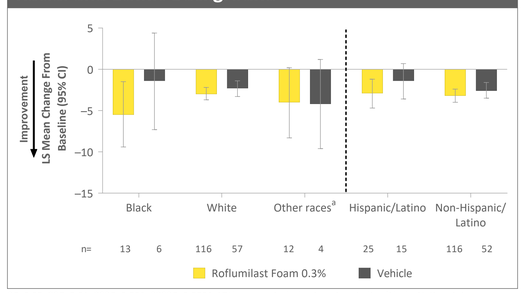
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
Scaling success defined as Scaling score of 0 (None) or 1 (Mild) plus a ≥2-grade improvement from baseline.
CI: confidence interval.

Figure 5. WI-NRS Success at Week 8 by Patient Racial and Ethnic Background



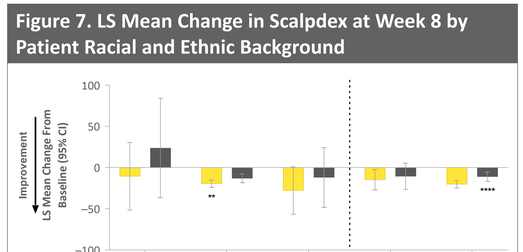
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
WI-NRS success defined as achievement of a ≥4-point improvement from baseline score of ≥4.
CI: confidence interval; WI-NRS: Worst Itch-Numeric Rating Scale.

Figure 6. LS Mean Change in DLQI at Week 8 by Patient Racial and Ethnic Background



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
CI: confidence interval; DLQI: Dermatology Life Quality Index; LS: least squares.

Figure 7. LS Mean Change in Scalpdex at Week 8 by Patient Racial and Ethnic Background



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. [a]Other races includes American Indian/Alaska Native, Asian, more than 1 race, or other.
CI: confidence interval; LS: least squares.

Safety

- Roflumilast foam was well tolerated and rates of AEs were low (Table 3)
  - ≥99% of roflumilast-treated and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator rating of local tolerability
  - Few treatment-related AEs were reported
  - Very few AEs led to study discontinuation, with similar rates of discontinuation between roflumilast and vehicle groups
  - No patients had a serious AE

Table 3. Overall AEs

n (%)	Roflumilast Foam 0.3% (n=154)	Vehicle (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 SAE	0 (0.0)	0 (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 (0.0)

[a]AEs leading to discontinuation for roflumilast were application-site pain, migraine, and dyspnea. In the vehicle group: application-site dysesthesia. [b]Contact dermatitis was reported to be unrelated to treatment in all cases; 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; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Safety: Hypopigmentation and Hyperpigmentation

- Most patients had no hyperpigmentation or hypopigmentation at any study visit
- At baseline, both hyper- and hypopigmentation were disproportionately more common in non-White patients
  - Most patients with hypopigmentation at baseline (11/226 [4.9%]) experienced full resolution (6/11; 54.5%) by Week 8
    - Hypopigmentation was more common in non-White patients (9/39; 23.1%) than White patients (2/180; 1.1%)
  - Most patients with hyperpigmentation at baseline (14/226 [6.8%]) experienced full resolution (11/14; 78.5%) by Week 8
    - Hyperpigmentation was more common in non-White patients (7/41; 17.1%) than White patients (7/180; 3.9%)
  - At Week 8, new instances of hypopigmentation (n=0) and hyperpigmentation (n=3, all White) were uncommon

CONCLUSIONS

- Once-daily roflumilast foam 0.3% demonstrated improvement in IGA score, erythema, scaling, itch, and quality of life
- Rates of treatment-related AEs, discontinuations due to AEs, and application-site pain were low and similar to that of vehicle
- Although the trial was not powered for racial and ethnicity subgroups and the subgroups were small, efficacy was consistent regardless of race and ethnicity

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DISCLOSURES

LHK, AFA, JAL, MB, ZDD, LKF, EL, CWL, AYM, LSG, PSY, MZ, and **SK** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **RCH, DK, PB,** and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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