Efficacy and Safety of Roflumilast Foam 0.3% in Patients With Seborrheic Dermatitis in a Randomized, Double-blind, Vehicle-Controlled Phase 2 Study

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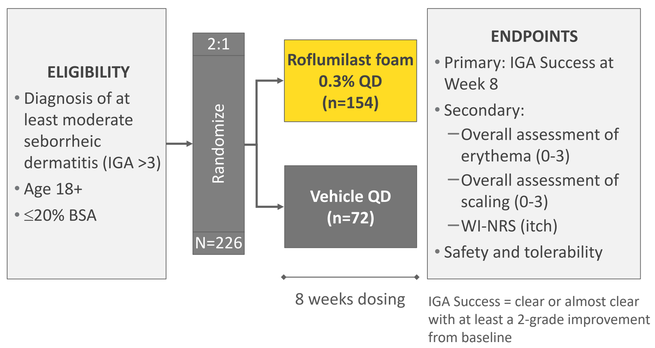
INTRODUCTION

- Seborrheic dermatitis (SD) is a chronic inflammatory skin condition that may cause physical discomfort and emotional burden for patients[1,2]
  - SD is characterized by erythematous, scaly plaques, with a yellowish, oily, moist, and/or greasy appearance and affects areas with abundant sebaceous glands[3,4]
- 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 potent, nonsteroidal, phosphodiesterase-4 inhibitor being investigated for once-daily treatment of several dermatologic conditions,[5] including SD
- A phase 2, 8-week study investigated using roflumilast foam 0.3% once daily for the treatment of SD (**Figure 1**; **Table 1**)

Figure 1. Study Design



BSA: body surface area; IGA: Investigator Global Assessment; QD: once daily; WI-NRS: Worst Itch-Numeric Rating Scale.

Table 1. Study Populations

n (%)	ARQ-154 0.3%	Vehicle	Vehicle (n=109)
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)
PRU2	141 (91.6)	68 (94.4)	209 (92.5)

*Excludes 2 subjects: One roflumilast subject (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 one vehicle subject (17006) who missed Week 8 IGA due to COVID-19, but did not discontinue due to COVID-19, and came back for the Week 9 visit.
ITT = all randomized subjects; safety population = all subjects who were enrolled and received at least 1 confirmed dose of IP; mITT = all randomized subjects except subjects who missed the Week 8 IGA assessment specifically due to COVID-19 disruption; PRU4 population = subset of ITT, includes subjects with WI-NRS pruritus score ≥4 at baseline; PRU2 population = subset of ITT, includes subjects with WI-NRS pruritus score ≥2 at baseline. IGA: Investigator Global Assessment; IP: investigational product; ITT: intent-to-treat; mITT: modified intent-to-treat; PRU: pruritus score at baseline; WI-NRS: Worst Itch-Numeric Rating Scale.

Table 2. Patient Disposition

n (%)	ARQ-154 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 subject	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)

RESULTS

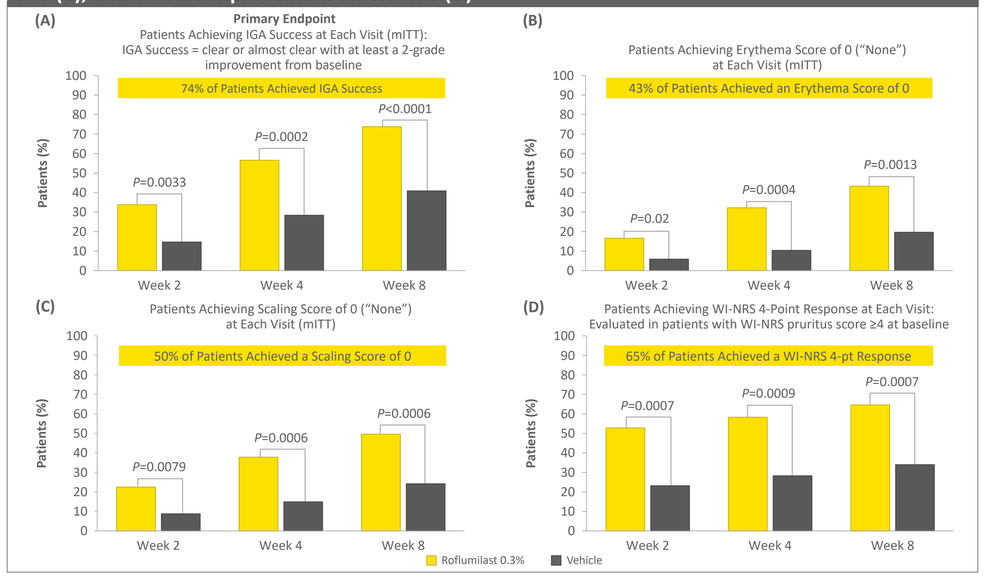
Table 3. Demographics and Baseline Characteristics (Safety Population)

n (%)	ARQ-154 0.3% (n=154)	Vehicle (n=72)	Overall (N=226)
Age, mean, years	45.3	44.2	44.9
Sex			
Male	76 (49.4)	40 (55.6)	116 (51.3)
Female	78 (50.6)	32 (44.4)	110 (48.7)
Ethnicity			
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			
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 1 race	5 (3.2)	1 (1.4)	6 (2.7)
BSA, mean (%)	3.3	3.0	3.2
Baseline IGA (0-4)			
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)			
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)			
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	125 (81.2)	59 (81.9)	184 (81.4)
Facial involvement	100 (64.9)	36 (50.0)	136 (60.2)

BSA: body surface area; IGA: Investigator Global Assessment; WI-NRS: Worst Itch-Numeric Rating Scale.

- Roflumilast foam 0.3% demonstrated significant and rapid improvement in SD, redness, scaling, and itch (**Figure 2**)

Figure 2. Percentages of Patients Achieving IGA Success (A), Erythema Score of 0 (B), Scaling Score of 0 (C), and 4-Point Improvement on WI-NRS (D)



mITT: all randomized patients except those who missed the Week 8 IGA assessment specifically due to COVID-19 disruption. IGA: Investigator Global Assessment; mITT: modified intent-to-treat; WI-NRS: Worst Itch-Numeric Rating Scale.

Safety

- Rates of adverse events (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. Safety

n (%)	Roflumilast 0.3% Foam (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 SAE	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

[a]AEs leading to discontinuation for roflumilast were application site pain, migraine, 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.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

SUMMARY AND 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)
- Rates of treatment-related AEs, discontinuations due to AEs, and application-site pain were low and similar to that of vehicle
- Once-daily roflumilast foam 0.3% provided safe, well-tolerated, and effective treatment of erythema, scaling, and itch caused by SD, and represents a promising novel treatment with early onset of action

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DISCLOSURES

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