Once-Daily Roflumilast Foam 0.3% for Scalp and Body Psoriasis: A Randomized, Double-blind, Vehicle-Controlled Phase 2b Study

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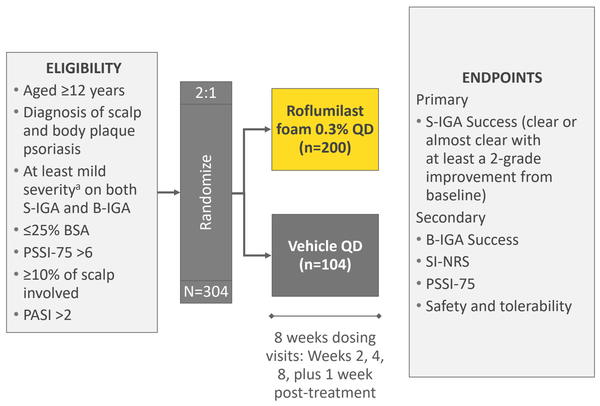
INTRODUCTION

- In patients with psoriasis, about 80% have scalp psoriasis (S-PsO)[1]
  - S-PsO is often associated with itch, the most burdensome symptom of psoriasis[2]
  - Itching, flaking, and appearance of plaques on the scalp can cause social embarrassment and adversely impact quality of life[3]
  - Treatment of S-PsO is difficult because the hair may limit efficacy of creams and ointments and reduce treatment adherence[4]
- Roflumilast is a potent, nonsteroidal, phosphodiesterase-4 inhibitor being investigated as a 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 S-PsO and body PsO in a phase 2, randomized, double-blind, vehicle-controlled 8-week study (**Figure 1**)

Figure 1. Study Design



[a]Protocol amendment 2: S-IGA entry criterion changed from ≥2 (mild) to ≥3 (moderate). [b]IGA Success = clear or almost clear with at least a 2-grade improvement from baseline.
BSA: body surface area; B-IGA: Body-Investigator Global Assessment; PASI: Psoriasis Area Severity Index; PSSI-75: Psoriasis Scalp Severity Index-75; QD: once daily; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Worst Itch-Numeric Rating Scale.

RESULTS

Table 1. Patient Disposition

n (%)	Roflumilast 0.3% (n=200)	Vehicle (n=104)	Overall (N=304)
Completed	177 (88.5)	87 (83.7)	264 (86.8)
Prematurely discontinued	23 (11.5)	17 (16.3)	40 (13.2)
Reason for discontinuation			
Withdrawal by subject	9 (4.5)	6 (5.8)	15 (4.9)
Noncompliance	1 (0.5)	0	1 (0.3)
Protocol violation	0	0	0
Lost to follow-up	8 (4.0)	7 (6.7)	15 (4.9)
Adverse event	5 (2.5)	2 (1.9)	7 (2.3)
Other	0	2 (1.9)	2 (0.7)

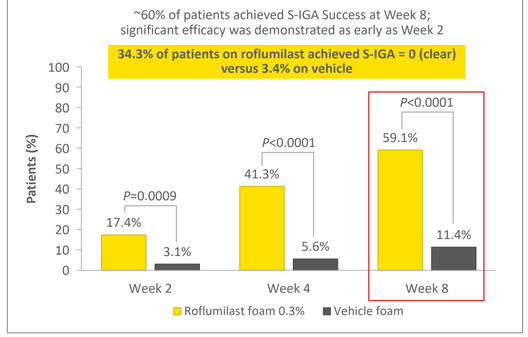
Table 2. Baseline Disease Characteristics (ITT Population)

n (%)	Roflumilast Foam 0.3% (n=200)[a]	Vehicle Foam (n=104)	Overall (N=304)
BSA, mean %	8.0	7.6	7.9
Baseline S-IGA			
2 – Mild	18 (9.0)	14 (13.5)	32 (10.5)
3 – Moderate	151 (75.5)	80 (76.9)	231 (76.0)
4 – Severe	29 (14.5)	10 (9.6)	39 (12.8)
Baseline B-IGA			
2 – Mild	69 (34.5)	39 (37.5)	108 (35.5)
3 – Moderate	119 (59.5)	60 (57.7)	179 (58.9)
4 – Severe	10 (5.0)	5 (4.8)	15 (4.9)
PSSI, mean (SD)	22.4 (12.5)	20.9 (11.7)	21.9 (12.3)
PASI, mean (SD)	7.2 (4.3)	6.8 (4.4)	7.0 (4.3)
SI-NRS, mean (SD)	6.4 (2.4)	6.6 (2.3)	6.5 (2.3)
SI-NRS, ≥4, n (%)	173 (86.5)	96 (92.3)	269 (88.5)

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

- Roflumilast foam significantly increased the percentage of patients with S-IGA Success at Week 8 (primary endpoint; **Figure 2**)

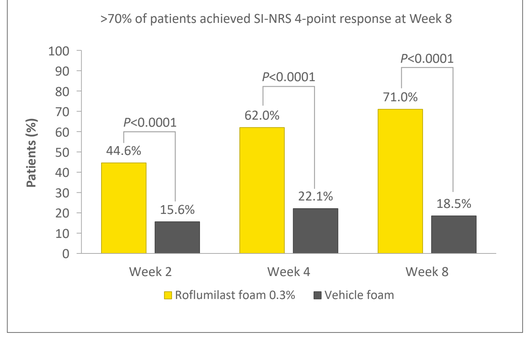
Figure 2. Percentage of Patients Achieving S-IGA Success



IGA Success: clear or almost clear with at least a 2-grade improvement from baseline. Intent-to-treat population. S-IGA: Scalp-Investigator Global Assessment.

- Significantly more roflumilast-treated patients had SI-NRS 4-point response as early as Week 2 (**Figure 4**)

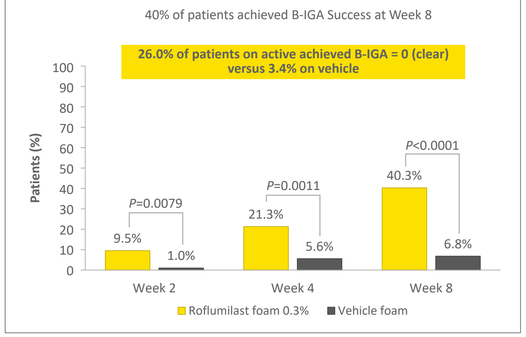
Figure 4. Percentage of Patients With SI-NRS Improvement ≥4 Points



Evaluated in patients with SI-NRS score ≥4 at baseline. Intent-to-treat population. SI-NRS: Scalp Worst Itch-Numeric Rating Scale.

- Significantly more patients treated with roflumilast foam had B-IGA Success as early as Week 2 (**Figure 3**)

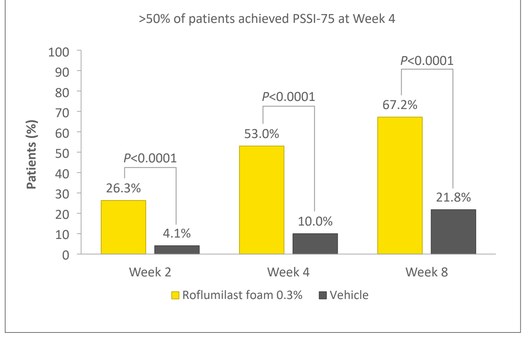
Figure 3. Percentage of Patients Achieving B-IGA Success



IGA Success: clear or almost clear with at least a 2-grade improvement from baseline. Intent-to-treat population. B-IGA: Body-Investigator Global Assessment.

- Significantly more roflumilast-treated patients achieved a 75% reduction in the Psoriasis Scalp Severity Index (PSSI-75; **Figure 5**)

Figure 5. Percentage of Patients Achieving PSSI-75



PSSI-75: Psoriasis Scalp Severity Index-75.

Safety

- Roflumilast foam had safety and tolerability profile similar to vehicle (**Table 3**)
- Rates of adverse events (AEs) were low
- Few treatment-related AEs were reported
- Only 1 patient had a serious AE (unrelated)
- Very few AEs led to study discontinuation
  - Discontinuation rates were similar between groups
- ≥99% of roflumilast-treated and ≥98% of vehicle-treated patients had no evidence of irritation on the investigator rating of local tolerability

Table 3. Safety

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 (0.0)
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 (0.0)

[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.
Data are presented for safety population. 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
  - Roflumilast foam provided a robust and rapid reduction in itch that was maintained 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

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