Patient-Reported Outcomes With Roflumilast Foam 0.3% in Patients With Scalp and Body Psoriasis in the Phase 3 ARRECTOR trial

Melinda Gooderham,[1] Jerry Bagel,[2] Seth B. Forman,[3] Leon Kircik,[4] Marni Wiseman,[5] Benjamin Lockshin,[6] Jennifer Soung,[7] David Krupa,[8] Saori Kato,[8] David R. Berk,[8] David H. Chu[8]

[1]SKiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [2]Psoriasis Treatment Center of Central New Jersey, East Windsor, NJ, USA; [3]ForCare Medical Center, Tampa, FL, USA; [4]Icahn School of Medicine at Mount Sinai, New York, NY, Indiana Medical Center, Indianapolis, IN, Physicians Skin Care, PLLC, and Skin Sciences, PLLC, Louisville, KY, USA; [5]SKiNWISE Dermatology, Probity Medical Research, and University of Manitoba, Winnipeg, MB, Canada; [6]DermAssociates, LLC, Rockville, MD, USA; [7]Southern California Dermatology, Santa Ana, CA, USA; [8]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

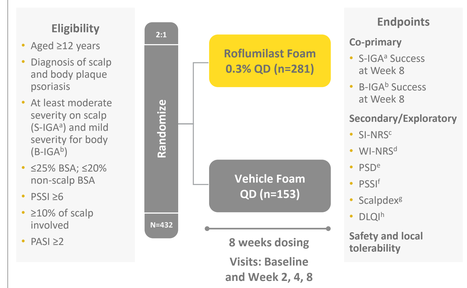
INTRODUCTION

- Plaque psoriasis is a chronic inflammatory skin condition that negatively impacts quality of life, including in patients in which the disease is not extensive[1]
  - Up to 80% of patients with psoriasis experience scalp psoriasis[2-4]
  - Disease severity scores may underestimate the impact of disease on overall quality of life[1]
- Roflumilast is a potent phosphodiesterase 4 (PDE4) inhibitor formulated as a water-based cream and foam
  - Roflumilast potency is ~25- to >300-fold higher than apremilast and crisaborole, with roflumilast more closely mimicking cyclic adenosine monophosphate (cAMP) binding to PDE4[5,6]
  - Formulations do not contain ethanol, propylene glycol, or fragrances that can irritate skin

METHODS

- ARRECTOR was a Phase 3, parallel-group, double-blind, vehicle-controlled trial (NCT05028582) enrolling patients ≥12 years of age with diagnosis of scalp and body psoriasis of at least moderate severity on the Scalp-Investigator Global Assessment (S-IGA) and mild severity on the Body-Investigator Global Assessment (B-IGA; **Figure 1**)
  - The co-primary efficacy endpoints were S-IGA Success and B-IGA Success at Week 8, which were defined as achievement of Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline
  - Patient-reported outcomes included Worst Itch Numeric Rating Scale (WI-NRS) and Scalp Itch Numeric Rating Scale (SI-NRS), Psoriasis Symptom Diary (PSD), Psoriasis Scalp Severity Index (PSSI), Scalpdex, and Dermatology Life Quality Index (DLQI)
  - Safety and local tolerability were also assessed

Figure 1. Study Design



S-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline
B-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline

[a]A 5-point scale (ranging from 0 [Clear] to 4 [Severe]) assessing severity of psoriasis on the scalp. [b]A 5-point scale (ranging from 0 [Clear] to 4 [Severe]) assessing severity of psoriasis on the body. [c]An 11-point scale assessing scalp itch, ranging from 0 (no itch) to 10 (worst itch imaginable). [d]An 11-point scale assessing itch of non-scalp body regions, ranging from 0 (no itch) to 10 (worst itch imaginable). [e]A 161-point scale assessing various psoriasis symptoms, including itch, pain, and scaling. [f]A 72-point scale based on psoriasis disease intensity and total affected body area. [g]A 23-item survey assessing quality of life in patients with scalp psoriasis. [h]A 30-point scale assessing patients' quality of life.
B-IGA: Body-Investigator Global Assessment; BSA: body surface area; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area and 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

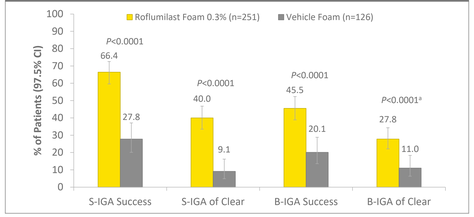
- Baseline disease characteristics were consistent between treatment groups (**Table 1**)
- Roflumilast provided significant improvement in scalp and body psoriasis, as indicated by improvements in S-IGA and B-IGA (**Figure 2**)

Table 1. Baseline Disease Characteristics

	Roflumilast Foam 0.3% (n=281)	Vehicle Foam (n=151)
Baseline S-IGA, mean (SD)	3.1 (0.4)	3.1 (0.3)
3 (Moderate), n (%)	239 (85.1)	131 (86.8)
4 (Severe), n (%)	42 (14.9)	20 (13.2)
Baseline B-IGA, mean (SD)	2.8 (0.5)	2.8 (0.5)
2 (Mild), n (%)	76 (27.0)	43 (28.5)
3 (Moderate), n (%)	191 (68.0)	99 (65.6)
4 (Severe), n (%)	14 (5.0)	9 (6.0)
SI-NRS, mean (SD)	5.8 (2.6)	6.1 (2.3)
WI-NRS, mean (SD)	5.7 (2.6)	5.5 (2.6)
PSD total score, mean (SD)	73.4 (40.2)	75.2 (36.9)
PSD aggregate score (itch/pain/scaling), mean (SD)	15.7 (7.3)	16.2 (6.7)
PSSI, mean (SD)	47.2 (22.9)	50.5 (20.4)
Scalpdex, mean (SD)	47.2 (22.9)	50.5 (20.4)
DLQI, mean (SD)	7.1 (5.3)	7.3 (4.8)
BSA (%), mean (SD)	6.1 (4.3)	6.0 (4.3)
Extent of scalp involvement (%), mean (SD)	34.4 (25.0)	36.0 (25.8)

SD: standard deviation.

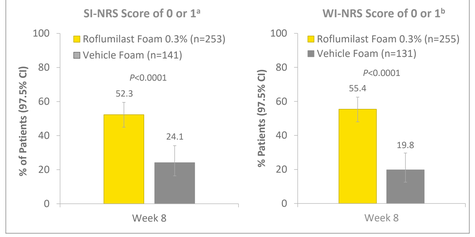
Figure 2. Percentage of Patients Achieving S-IGA Success, S-IGA of Clear, B-IGA Success, and B-IGA of Clear at Week 8



Multiple imputation of missing data.
[a]Nominal *P* value.
CI: confidence interval.

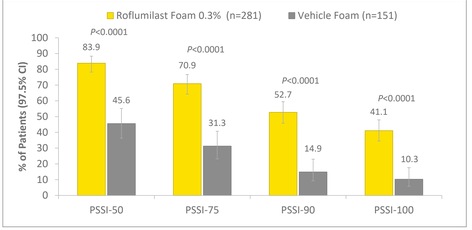
- Once-daily treatment with roflumilast foam 0.3% also resulted in significant improvement in patient-reported outcomes
- In patients with SI-NRS and WI-NRS ≥2 at baseline, more roflumilast-treated than vehicle-treated patients achieved a score of 0 or 1 at Week 8 (**Figure 3**)
- At Week 8, significantly more roflumilast-treated than vehicle-treated patients achieved a PSD total score of 0 (19.6% vs 7.1%; *P*=0.0002)
  - Least squares (LS) mean change from baseline (CfB) in PSD items related to itching/pain/scaling was significantly greater with roflumilast than with vehicle at Week 8 (LS mean CfB: −10.87 vs −5.75; *P*<0.0001)
- Significantly more roflumilast-treated than vehicle-treated patients achieved 50%, 75%, and 90% reductions in PSSI scores (**Figure 4**)
- At Week 8, LS mean CfB in Scalpdex total score was also significantly greater with roflumilast than with vehicle (**Figure 5**)
- Roflumilast treatment also resulted in a significantly greater LS mean CfB in DLQI score at Week 8 (roflumilast: −2.86, n=276; vehicle: −1.99, n=149; *P*<0.0001)

Figure 3. Improvement in Scalp and Body Pruritus at Week 8



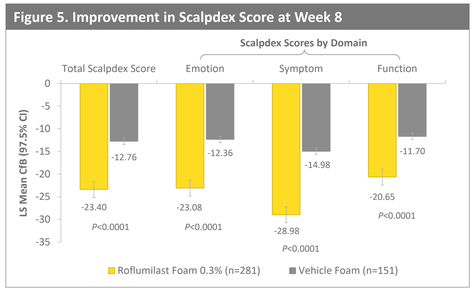
[a]SI-NRS score of 0 or 1 evaluated in patients with baseline SI-NRS ≥2.
[b]WI-NRS score of 0 or 1 evaluated in patients with baseline WI-NRS ≥2.
CI: confidence interval.

Figure 4. Percentage of Patients Achieving PSSI Responses at Week 8



Multiple imputation of missing data. PSSI-50/75/90/100: 50%/75%/90%/100% reduction in PSSI from baseline.
CI: confidence interval.

Figure 5. Improvement in Scalpdex Score at Week 8



Missing data were not imputed.
CfB: change from baseline; CI: confidence interval; LS: least squares.

- A series of photographs of a patient with improvement in psoriasis following roflumilast treatment is shown in **Figure 6**

Figure 6. Improvement in Patient With Psoriasis Treated With Roflumilast Foam 0.3%

A

Baseline	Week 2	Week 4	Week 8
S-IGA: 4 PSSI: 18 SI-NRS: 9	S-IGA: 3 PSSI: 18 SI-NRS: 4	S-IGA: 1 PSSI: 1 SI-NRS: 2	S-IGA: 1 PSSI: 1 SI-NRS: 0

56-year-old male, Black or African American/Not Hispanic or Latino

B

Baseline	Week 2	Week 4	Week 8
S-IGA: 4 PSSI: 55 SI-NRS: 8	S-IGA: 3 PSSI: 20 SI-NRS: 4	S-IGA: 2 PSSI: 8 SI-NRS: 2	S-IGA: 1 PSSI: 2 SI-NRS: 0

57-year-old male, White/Not Hispanic or Latino

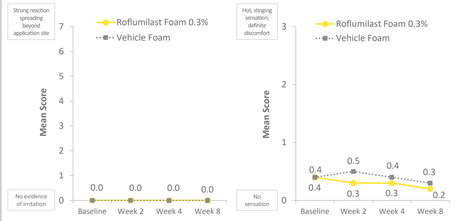
- Incidence of treatment-emergent adverse events was low in both treatment groups (**Table 2**)
- Investigator- and patient-rated local tolerability was favorable (**Figure 7**)

Table 2. Safety

n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle Foam (n=151)
Patients with any TEAE	75 (26.7)	25 (16.6)
Patients with any treatment-related TEAE	16 (5.7)	3 (2.0)
Patients with any treatment-emergent SAE	2 (0.7)	1 (0.7)
Patients with any treatment-related SAE	1 (0.4)	0
Patients who discontinued trial drug due to an AE	7 (2.5)	2 (1.3)
Patients who discontinued trial due to AE	5 (1.8)	2 (1.3)
Most common TEAEs by Preferred Term, ≥1% in any group		
Headache	13 (4.6)	3 (2.0)
Diarrhea	9 (3.2)	4 (2.6)
COVID-19	8 (2.8)	4 (2.6)
Nasopharyngitis	4 (1.4)	2 (1.3)
Nausea	6 (2.1)	0
Hypertension	3 (1.1)	2 (1.3)
Urinary tract infection	2 (0.7)	2 (1.3)
Upper respiratory tract infection	3 (1.1)	0

SAEs include bipolar disorder (roflumilast; unrelated); gastritis (roflumilast; possibly related); joint dislocation, peripheral artery occlusion, and radius fracture (vehicle; all unrelated)
AE: adverse event; COVID-19: coronavirus disease 2019; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Figure 7. (A) Investigator- and (B) Patient-Rated Local Tolerability



Scale for investigator-rated local tolerability (0–7)
0 = no evidence of irritation; 1 = minimal erythema, barely perceptible; 2 = definite erythema, readily visible; minimal edema or minimal papular response; 3 = erythema and papules; 4 = definite edema; 5 = erythema, edema, and papules; 6 = vesicular eruption; 7 = strong reaction spreading beyond application site

Scale for patient-rated local tolerability (0–3)
0 (none) = no sensation; 1 (mild) = slight warm, tingling sensation; not really bothersome; 2 (moderate) = definite warm, tingling sensation that is somewhat bothersome; 3 (severe) = hot, tingling/stinging sensation that has caused definite discomfort

CONCLUSION

- In patients with scalp and body psoriasis, treatment with once-daily roflumilast foam 0.3% demonstrated greater improvement compared with vehicle across multiple patient-reported efficacy endpoints
  - Significant improvement in both scalp and body psoriasis occurred as early as 2 weeks after treatment initiation, the first time point measured
  - Significant improvement in patient-reported outcomes occurred, indicating relief from itching, pain, and scaling that was associated with improved quality of life
- Safety and local tolerability were favorable

REFERENCES

1. Stern RS, et al. *J Investig Dermatol Symp Proc* 2004;9:136–139.
2. Callis Duffin K, et al. *Dermatology* 2021;237:46–55.
3. Egeberg A, et al. *BMC Dermatol* 2020;20:3.
4. van de Kerkhof PC, et al. *Dermatology* 1998;197:31–36.
5. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
6. Wang J, Bunick CG. International Societies for Investigative Dermatology (ISID) Meeting 2023.

ACKNOWLEDGMENTS

- Thank you to the investigators and their staff for their participation in the trial. We are grateful to the study participants and their families for their time and commitment. Writing support was provided by Christina McManus, PhD, CMPP, and Ashley Oney, MD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

MG, JB, SBF, LK, MW, BL, and JS are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DK, SK, DRB, and DHC are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.