Pooled Efficacy and Safety Results From the DERMIS-1 and DERMIS-2 Phase 3 Trials of Once-Daily Roflumilast Cream 0.3% by Baseline Body Surface Area

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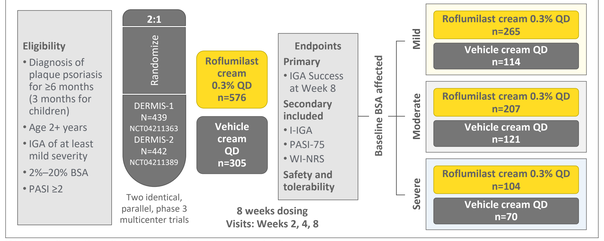
INTRODUCTION

- Roflumilast is a selective and highly potent phosphodiesterase-4 (PDE-4) inhibitor with greater affinity for PDE-4 than apremilast or crisaborole and approximately 25- to >300-fold more potent based on in vitro assays[1]
- Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for various dermatologic conditions, including psoriasis, atopic dermatitis, seborrheic dermatitis, and scalp psoriasis
- In a phase 2b, randomized, double-blind, vehicle-controlled trial, roflumilast cream provided significant improvement of psoriasis, including reduction of itch as early as Week 2 post-treatment, the first timepoint measured[2]
- Roflumilast cream 0.3% was evaluated in 2 identical, randomized, double-blind, vehicle-controlled phase 3 trials in patients ≥2 years of age with psoriasis involving 2%–20% body surface area (BSA), DERMIS-1 and DERMIS-2[3]
- In this poster, we present pooled efficacy and safety data from DERMIS-1 and DERMIS-2 analyzed by baseline BSA affected (mild [<5%], moderate [5%–10%], and severe [>10%])

METHODS

- DERMIS-1 and DERMIS-2 were 2 identical, phase 3, randomized, double-blind, vehicle-controlled studies of once-daily roflumilast cream 0.3% in patients with psoriasis (**Figure 1**)
- The primary efficacy endpoint was Investigator Global Assessment (IGA) Success at Week 8, which was defined as achievement of Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline

Figure 1. Study Design



IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous-IGA; PASI-75: 75% reduction in Psoriasis Area Severity Index; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

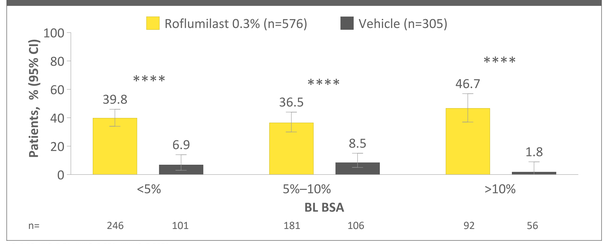
- Baseline disease characteristics and demographics were similar across treatment groups (**Table 1**)
- More roflumilast-treated patients achieved IGA Success at Week 8, and rates were generally consistent across all BSA categories (**Figure 2**)
- Treatment differences favored roflumilast versus vehicle for percentages of patients with intertriginous IGA Success (**Figure 3**), 75% reduction in Psoriasis Area Severity Index score (PASI-75; **Figure 4**), and Worst Itch Numeric Rating Scale (WI-NRS) Success across BSA categories (**Figure 5**)
- Rates of treatment-related adverse events (AEs) and discontinuations due to AEs were comparable with vehicle across all BSA categories (**Table 2**)
  - Rates of diarrhea suggest an association with baseline disease severity
- Overall local tolerability of roflumilast cream was assessed by patients and investigators
  - On investigator-rated local tolerability, more than 97% of patients in each treatment group had no signs of irritation at Week 4 or Week 8
  - More than 99% of patients reported no or mild sensation after applying roflumilast cream at Week 4 and Week 8, similar to that of vehicle

Table 1. Baseline Demographics and Disease Characteristics

	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
Age in years, mean (SD)	47.2 (14.6)	47.9 (15.0)
Sex		
Male, n (%)	365 (63.4)	196 (64.3)
Female, n (%)	211 (36.6)	109 (35.7)
Race, n (%)		
American Indian or Alaska Native	4 (0.7)	2 (0.7)
Asian	41 (7.1)	20 (6.6)
Black or African American	21 (3.6)	17 (5.6)
Native Hawaiian or Other Pacific Islander	5 (0.9)	1 (0.3)
White	474 (82.3)	250 (82.0)
Not reported	9 (1.6)	5 (1.6)
Other	19 (3.3)	9 (3.0)
More than 1 race	3 (0.5)	1 (0.3)
IGA score, n (%)		
2 (mild)	101 (17.5)	44 (14.4)
3 (moderate)	426 (74.0)	240 (78.7)
4 (severe)	49 (8.5)	21 (6.9)
Psoriasis-affected BSA, mean % (SD)	6.7 (4.6)	7.6 (4.9)
BSA category, n (%)		
<5%	265 (46.0)	114 (37.4)
5%–10%	207 (35.9)	121 (39.7)
>10%	104 (18.1)	70 (23.0)
PASI, mean score (SD)	6.4 (3.2)	6.9 (3.6)
WI-NRS, mean score (SD)	5.7 (2.7)	5.9 (2.8)
WI-NRS score ≥4, n (%)	447 (77.6)	231 (75.7)

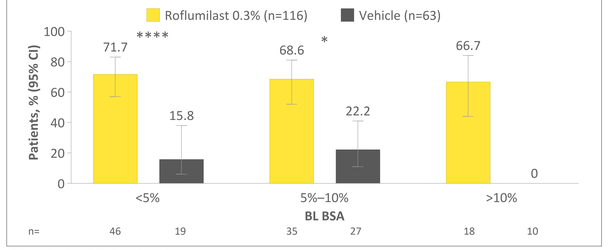
BSA: body surface area; IGA: Investigator Global Assessment; PASI: Psoriasis Area Severity Index; WI-NRS: Worst Itch Numeric Rating Scale; SD: standard deviation.

Figure 2. Percentage of Patients Achieving IGA Success at Week 8 by Baseline BSA



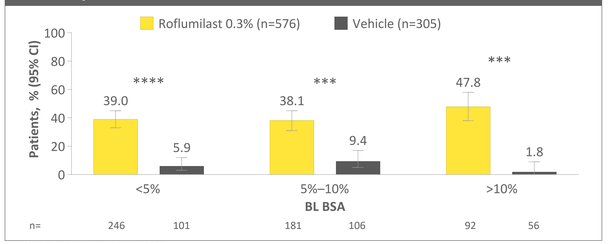
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
BL: baseline; BSA: body surface area; CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Percentage of Patients Achieving I-IGA Success at Week 8 by Baseline BSA



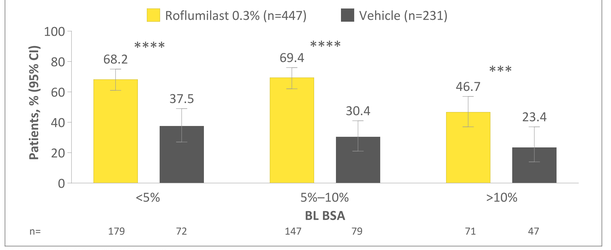
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
I-IGA Success = Clear or Almost Clear I-IGA status plus ≥2-grade improvement from baseline.
BL: baseline; BSA: body surface area; CI: confidence interval; I-IGA: Intertriginous-Investigator Global Assessment.

Figure 4. Percentage of Patients Achieving 75% Reduction in PASI (PASI-75) at Week 8 by Baseline BSA



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
BL: baseline; BSA: body surface area; CI: confidence interval; PASI-75: 75% reduction in Psoriasis Area Severity Index.

Figure 5. Percentage of Patients Achieving WI-NRS Success at Week 8 by Baseline BSA



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4.
BL: baseline; BSA: body surface area; CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Table 2. Adverse Events

	BSA <5%		BSA 5%–10%		BSA >10%	
n (%)	Roflumilast Cream 0.3% (n=265)	Vehicle (n=114)	Roflumilast Cream 0.3% (n=207)	Vehicle (n=121)	Roflumilast Cream 0.3% (n=104)	Vehicle (n=70)
Patients with any TEAE	67 (25.3)	31 (27.2)	51 (24.6)	19 (15.7)	29 (27.9)	14 (20.0)
Patients with any treatment-related TEAE	8 (3.0)	3 (2.6)	7 (3.4)	5 (4.1)	8 (7.7)	3 (4.3)
Patients with any serious AE	0	1 (0.9)	2 (1.0)	1 (0.8)	0	0
Patients who discontinued study due to AE	1 (0.4)	2 (1.8)	3 (1.4)	2 (1.7)	2 (1.9)	0
Most common TEAE (>2% in any group), preferred term						
Hypertension[a]	3 (1.1)	4 (3.6)	3 (1.4)	1 (0.8)	3 (2.9)	1 (1.4)
Headache	6 (2.3)	2 (1.8)	3 (1.4)	1 (0.8)	5 (4.8)	0
Diarrhea	3 (1.1)	0	8 (3.9)	0	7 (6.7)	0
Nausea	0	0	5 (2.4)	1 (0.8)	2 (1.9)	0
Insomnia	1 (0.4)	1 (0.9)	4 (1.9)	0	3 (2.9)	1 (1.4)
Pruritus	0	1 (0.9)	0	0	3 (2.9)	0
Pyrexia	2 (0.8)	0	0	0	1 (1.0)	2 (2.9)

[a]Hypertension includes synonymous terms (eg, blood pressure increased). Data are presented for safety population.
AE: adverse event; BSA: body surface area; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- In a pooled analysis of DERMIS-1 and DERMIS-2, once-daily roflumilast cream demonstrated consistent efficacy and itch reduction at Week 8 regardless of baseline disease severity
- Roflumilast cream demonstrated favorable local tolerability and low rates of treatment-emergent AEs, serious AEs, and discontinuations due to AEs
- These phase 3 studies demonstrated that investigational, once-daily roflumilast cream 0.3% has the potential to address many of the shortcomings of existing topical treatments for plaque psoriasis regardless of baseline disease severity

REFERENCES

1. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
2. Lebwohl MG, et al. *N Engl J Med* 2020;383:229–239.
3. Lebwohl MG, et al. European Academy of Dermatology & Venereology (EADV) Symposium 2021.

DISCLOSURES

LSG, **JB**, **JD**, **LJG**, **ML**, and **LHK** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **AF**, **SS**, **RCH**, **PB**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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