Pooled Efficacy and Safety Results From the DERMIS-1 and DERMIS-2 Phase 3 Trials of Once-Daily Roflumilast Cream 0.3% for Treatment of Chronic Plaque Psoriasis

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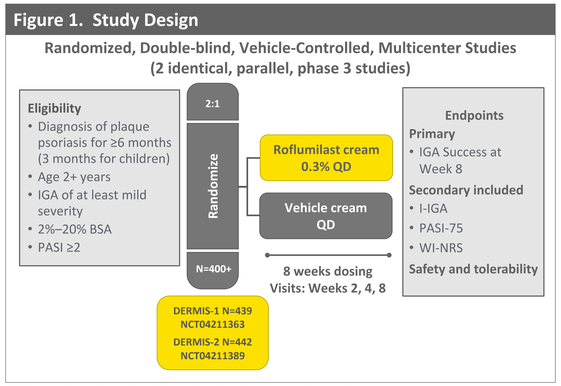
INTRODUCTION

- Recent prevalence estimates suggest that 78% of patients with psoriasis in the United States have mild to moderate disease (<10% body surface area [BSA]),[1] for which topical therapy is considered first-line therapy[2]; however, no novel nonsteroidal topical therapies for plaque psoriasis have been approved in more than 2 decades
  - Various topical treatments are available for chronic plaque psoriasis, such as corticosteroids, vitamin D derivatives, and calcineurin inhibitors; however, there remains an unmet need for effective therapies that are safe and well-tolerated for long-term use[3]
- 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[4]
- Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for various dermatologic conditions, including atopic dermatitis, seborrheic dermatitis, and scalp psoriasis
- Efficacy, safety, and tolerability of roflumilast cream in psoriasis have been demonstrated in a phase 2b study in patients with psoriasis and the individual phase 3 DERMIS-1 and DERMIS-2 results were previously reported[5,6]
- Here, we report the pooled efficacy and safety results from DERMIS-1 and DERMIS-2

METHODS

- DERMIS-1 and DERMIS-2 were 2 identical, phase 3, randomized, double-blind, vehicle-controlled, 8-week studies of once-daily roflumilast cream 0.3% in patients (≥2 years of age) with psoriasis (affected BSA 2%–20%; **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; IG: 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

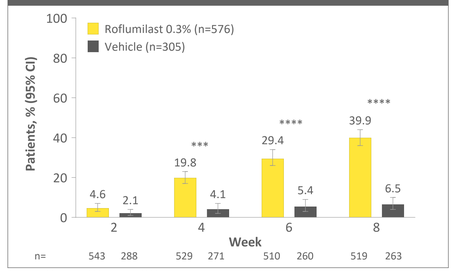
- Baseline disease characteristics and demographics were similar across treatment groups (**Table 1**)
- Significantly more roflumilast-treated patients achieved the primary endpoint, IGA Success at Week 8 (**Figure 2**)
  - Significantly greater percentages of patients in the roflumilast group had IGA Success at other timepoints compared with that of the vehicle group
  - More patients in the roflumilast group also had an IGA status of Clear or Almost Clear at all timepoints (**Figure 3**)
- Significantly more roflumilast-treated patients had intertriginous IGA (I-IGA) Success (**Figure 4**), a 75% reduction in Psoriasis Area Severity Index (PASI-75) score (**Figure 5**), and Worst Itch Numeric Rating Scale (WI-NRS) Success (**Figure 6**)

Table 1. Baseline Demographics and Disease Characteristics

n (%)	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)
I-IGA score, n (%)		
1 (almost clear)	7 (1.2)	2 (0.7)
2 (mild)	58 (10.1)	29 (9.5)
3 (moderate)	54 (9.4)	33 (10.8)
4 (severe)	4 (0.7)	1 (0.3)
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)

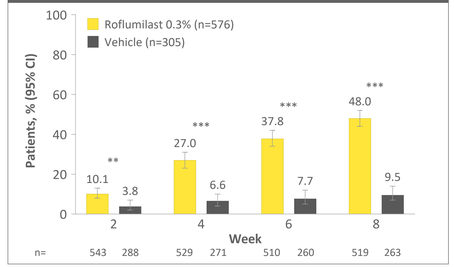
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous IGA; PASI: Psoriasis Area Severity Index; WI-NRS: Worst Itch Numeric Rating Scale; SD: standard deviation.

Figure 2. Percentage of Patients Achieving IGA Success



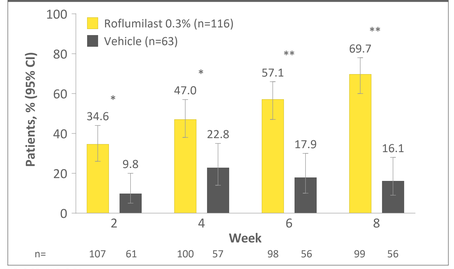
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 3. Percentage of Patients Achieving IGA Status of Clear or Almost Clear



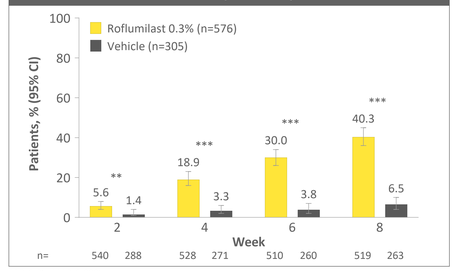
**P<0.01; ***P<0.0001.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 4. Percentage of Patients Achieving I-IGA Success



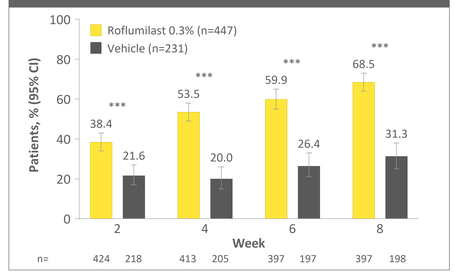
*P<0.05; **P<0.01.
I-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
CI: confidence interval; I-IGA: Intertriginous Investigator Global Assessment.

Figure 5. Percentage of Patients Achieving 75% Reduction in PASI Scores (PASI-75)



**P<0.01; ***P<0.0001.
CI: confidence interval; PASI-75: 75% reduction in Psoriasis Area Severity Index.

Figure 6. Percentage of Patients Achieving WI-NRS Success



***P<0.0001.
WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4.
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Safety

- Roflumilast cream demonstrated low rates of application-site adverse events (AEs), treatment-related AEs, and discontinuations due to AEs, comparable with vehicle (**Table 2**)
- There were no treatment-related serious AEs

Local Tolerability

- On investigator-rated local tolerability, more than 97% of patients in each 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 with that of vehicle

Table 2. Adverse Events

n (%)	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
Patients with any TEAE	147 (25.5)	64 (21.0)
Patients with any treatment-related TEAE	23 (4.0)	11 (3.6)
Patients with any SAE	2 (0.3)	2 (0.7)
Patients who discontinued study due to AE	6 (1.0)	4 (1.3)
Most common TEAE (≥1% in the roflumilast group), preferred term		
Diarrhea	18 (3.1)	0
Headache	14 (2.4)	3 (1.0)
Insomnia	8 (1.4)	2 (0.7)
Nausea	7 (1.2)	1 (0.3)
Nasopharyngitis	6 (1.0)	4 (1.3)
Urinary tract infection	6 (1.0)	2 (0.7)
Application-site pain	6 (1.0)	1 (0.3)
Upper respiratory tract infection	6 (1.0)	1 (0.3)

AE: adverse event; BSA: body surface area; SAE: serious adverse event; SD: standard deviation; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Roflumilast cream 0.3% demonstrated statistically significant improvements on endpoints assessing disease severity, including intertriginous areas, and pruritus
- The local tolerability profile as assessed by both patients and investigators was favorable
- The pooled results of the phase 3 DERMIS-1 and DERMIS-2 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

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DISCLOSURES

ML, **MJG**, **STG**, **HCH**, **LHK**, **AYM**, and **MZ** are an investigator and/or consultant for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **AF**, **RCH**, **PB**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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