Efficacy and Tolerability of Roflumilast Cream 0.3% in Patients With Chronic Plaque Psoriasis Involvement on the Face, Intertriginous, or Genital Areas: Pooled Results From Phase 3 Trials (DERMIS-1 and DERMIS-2)

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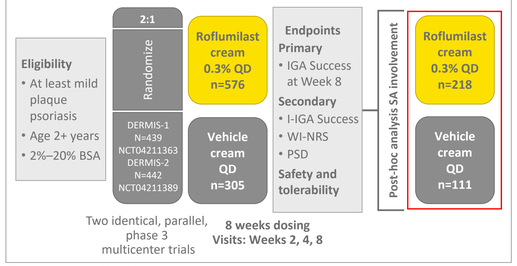
INTRODUCTION

- Patients with psoriasis involving special areas, such as the face, intertriginous, and genital areas, may have a disproportionately greater negative impact on their quality of life than patients without psoriasis involvement in those areas[1]
- Chronic use of current topical treatment options in these areas is limited due to risk of local skin side effects or limitations on duration of use[2]
- Roflumilast is a selective and highly potent phosphodiesterase 4 (PDE4) inhibitor with greater affinity for PDE4 than apremilast or crisaborole and approximately 25- to >300-fold more potent based on in vitro assays[3]
  - Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for long-term management of various dermatologic conditions, including atopic dermatitis, seborrheic dermatitis, and chronic plaque psoriasis (approved by the US Food and Drug Administration July 29, 2022)
- Efficacy, safety, and tolerability of roflumilast cream 0.3% in psoriasis have been demonstrated in a phase 2b study in patients with psoriasis; the individual phase 3 DERMIS-1 and DERMIS-2 results were previously reported[4,5]
- Here, we report the pooled results from 2 phase 3, randomized, double-blind, vehicle-controlled, multicenter trials of once-daily roflumilast cream 0.3% in patients with psoriasis (DERMIS-1 and DERMIS-2), presenting subgroup analyses of patients with involvement of special areas (SAs: defined as the face, and/or intertriginous, and/or genital areas)

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 (body surface area [BSA] affected: 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; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; PSD: Psoriasis Symptoms Diary; QD: once daily; SA: special areas (SA: defined as the face, and/or intertriginous, and/or genital areas); WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

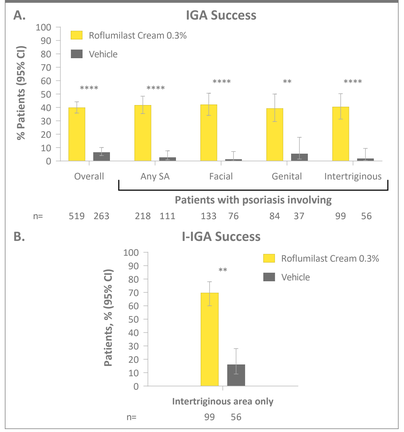
- Baseline disease characteristics and demographics were similar across treatment groups (**Table 1**)
- Significantly more roflumilast-treated patients achieved the primary endpoint, IGA Success at Week 8 (**Figure 2**)
  - Across the subgroups at Week 8, a greater percentage of patients in the roflumilast group achieved IGA Success compared with that of the vehicle group
  - More patients in the roflumilast group also had an IGA status of Clear or Almost Clear across subgroups at Week 8 (**Figure 3**)
- More roflumilast-treated patients who had a baseline score ≥4 on the Worst Itch Numeric Rating Scale (WI-NRS) had a 4-point improvement at Week 8 across subgroups (**Figure 4**)
- The least square mean percent change from baseline in Psoriasis Symptoms Diary (PSD) scores was greater after roflumilast treatment than with vehicle treatment at Week 8 across subgroups (**Figure 5**)

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, n (%)		
Male	365 (63.4)	196 (64.3)
Female	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)

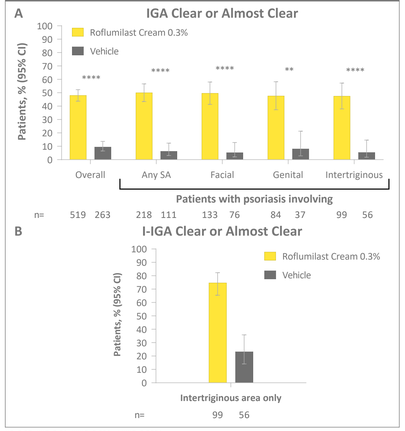
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; PASI: Psoriasis Area Severity Index; WI-NRS: Worst Itch Numeric Rating Scale; SD: standard deviation.

Figure 2. Percent of Patients With Involvement in SAs Achieving IGA Success (A) and I-IGA Success (B) at Week 8



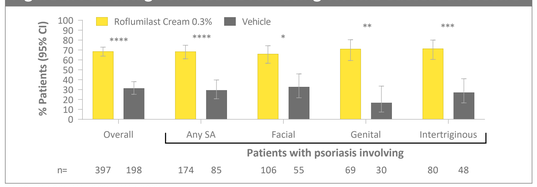
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline; I-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline evaluated in intertriginous areas only.
CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: Intertriginous-IGA; SA: special areas.

Figure 3. Percent of Patients With Involvement in SAs Achieving IGA Status of Clear or Almost Clear (A) and I-IGA Clear or Almost Clear (B) at Week 8



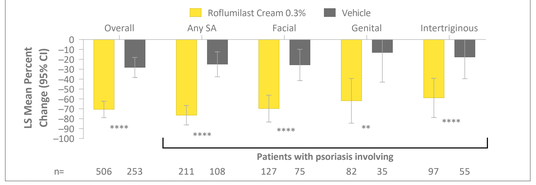
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
I-IGA Clear or Almost Clear IGA status evaluated in intertriginous areas only.
CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: Intertriginous IGA; SA: special area.

Figure 4. Percentage of Patients Achieving WI-NRS Success at Week 8



*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.
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 5. LS Mean Percent Change in PSD at Week 8



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
CI: confidence interval; LS: least square; PSD: Psoriasis Symptoms Diary.

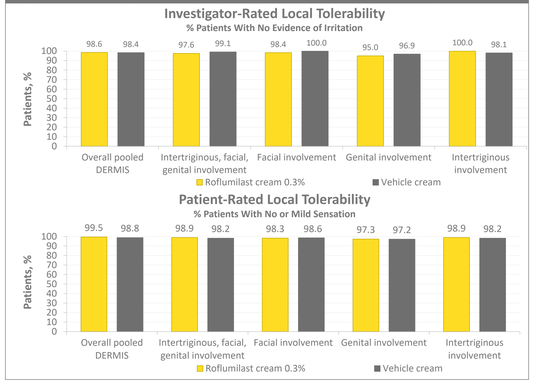
Safety

- In patients with involvement in SA, local tolerability was highly favorable as reported by patient and investigator assessment of irritation, burning, and stinging (**Figure 6**)
  - ≥97.6% of patients had no evidence of irritation at Week 8 on investigator-rated assessments
  - ≥97.2% reported no warmth/tingling sensation or mild sensation at Week 8 on patient-rated assessments
- Overall incidence of treatment-emergent adverse events (TEAEs), serious AEs, and TEAEs leading to discontinuation was low with similar rates between roflumilast and vehicle across both studies
- No skin atrophy was seen in the SAs treated with topical roflumilast or vehicle (**Table 2**)

CONCLUSIONS

- Roflumilast cream 0.3% provided improvement across multiple efficacy endpoints versus vehicle cream while demonstrating favorable safety and tolerability in patients with chronic plaque psoriasis involving intertriginous, and/or face, and/or genital areas in 2 phase 3 trials
- The local tolerability profile as assessed by both patients and investigators was favorable
- The subgroup analysis of the pooled results of the phase 3 DERMIS-1 and DERMIS-2 trials showed that once-daily roflumilast cream 0.3% demonstrated efficacy and tolerability in patients with psoriasis involvement in difficult-to-treat areas

Figure 6. Investigator- and Patient-Rated Local Tolerability at Week 8



Patient-rated tolerability: 0 = None (no sensation), 1 = Mild (slight warm, tingling sensation), 2 = Moderate (definite warm, tingling sensation), 3 = Severe (hot, tingling/stinging sensation).

Table 2. Overall AEs[6]

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; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

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DISCLOSURES

LKF, **AA**, **JD**, **ZDD**, **MG**, **ML**, **KAP**, **JS**, and **LSG** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **DK**, **RCH**, **PB**, and **DRB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.