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)

Laura K. Ferris,[1] April Armstrong,[2] James Del Rosso,[3] Zoe D. Draelos,[4] Melinda Gooderham,[5] Mark Lebwohl,[6] Kim A. Papp,[7] Jennifer Soung,[8] Linda Stein Gold,[9] David Krupa,[10] Robert C. Higham,[10] Patrick Burnett,[10] David R. Berk[10]

[1]University of Pittsburgh, Department of Dermatology, Pittsburgh, PA, USA; [2]Keck School of Medicine, Department of Dermatology, University of Southern California Los Angeles, CA, USA; [3]JDR Dermatology Research Center, LLC, Las Vegas, NV, USA; [4]Dermatology Consulting Services, High Point, NC, USA; [5]SkiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [7]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [8]Southern California Dermatology, Santa Ana, CA, USA; [9]Henry Ford Medical Center, Detroit, MI, USA; [10]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

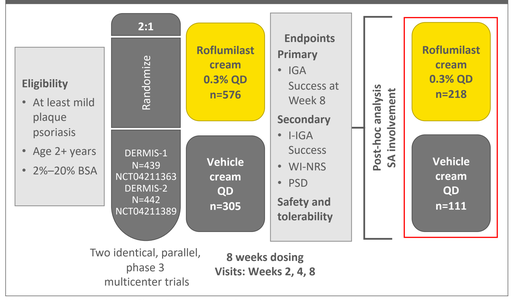
INTRODUCTION

- 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

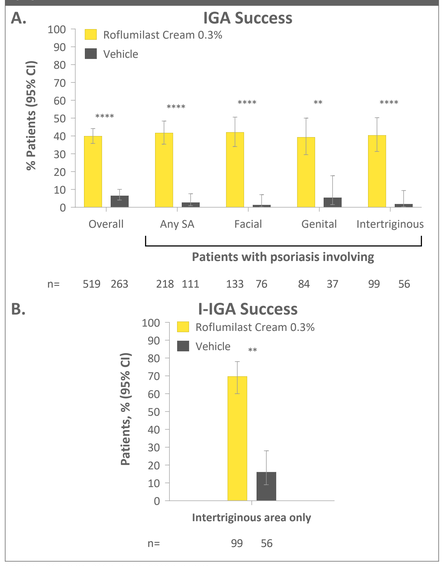
- Baseline disease characteristics and demographics were similar across treatment groups (Table 1)
- Significantly more roflumilast-treated patients achieved the primary endpoint, IGA Success at Week 8 (Figure 2)
  - Across the subgroups at Week 8, a greater percentage of patients in the roflumilast 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)

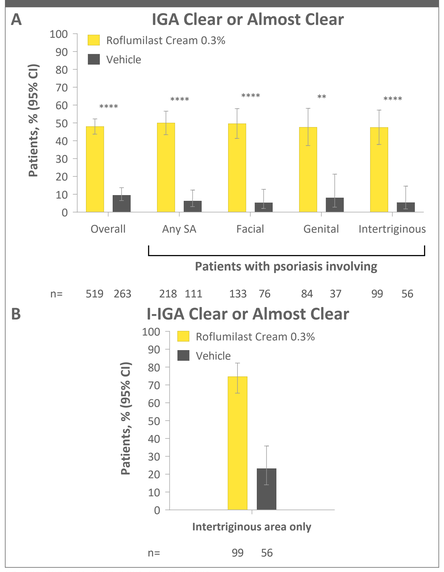
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; PASI: Psoriasis Area Severity Index; WI-NRS: Worst Itch Numeric Rating Scale; SD: standard deviation.

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



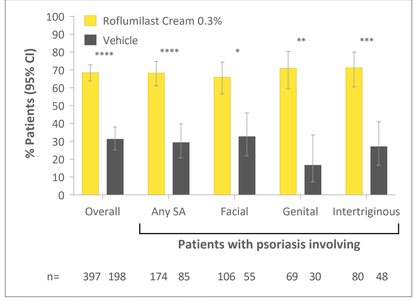
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline; I-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline evaluated in intertriginous areas only.
CI: confidence interval; IGA: Investigator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



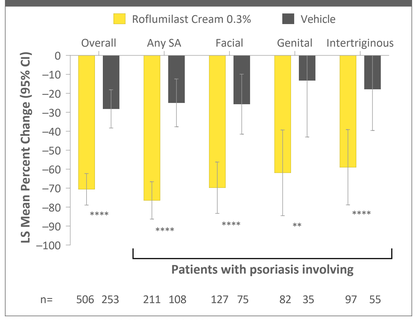
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
I-IGA Clear or Almost Clear IGA status evaluated in intertriginous areas only.
CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; SA: special area.

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

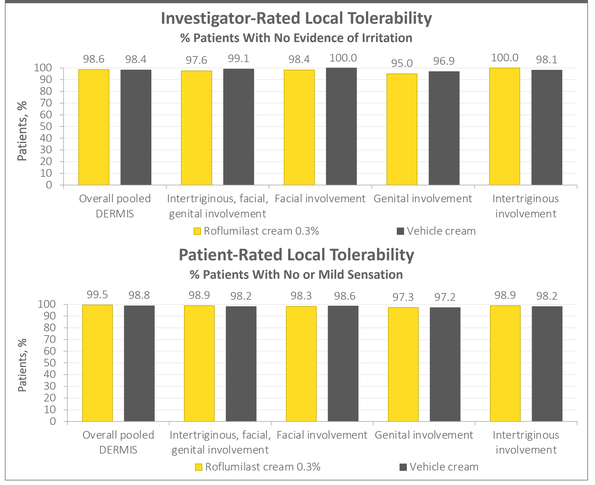


*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
CI: confidence interval; LS: least square; PSD: Psoriasis Symptoms Diary.

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

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).

- 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)

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.

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

REFERENCES

1. Merola JF, et al. *Dermatol Ther* 2018;31:e12589.
2. Elmets CA, et al. *J Am Acad Dermatol* 2021;84:432–470.
3. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
4. Lebwohl MG, et al. *N Engl J Med* 2020;383: 229–239.
5. Lebwohl MG, et al. 30th Congress of the European Academy of Dermatology and Venereology (EADV) Virtual, September 29–October 2, 2021.
6. Lebwohl MG, et al. American Academy of Dermatology (AAD), Boston, MA, March 25–29, 2022.

ACKNOWLEDGEMENTS

• This study was supported by Arcutis Biotherapeutics, Inc.
• 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, and Lauren Ramsey, PharmD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

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.