Long-term Safety and Efficacy of Roflumilast Cream 0.3% in Patients With Chronic Plaque Psoriasis: Interim Results From a 24-Week, Phase 3 Open-Label Study

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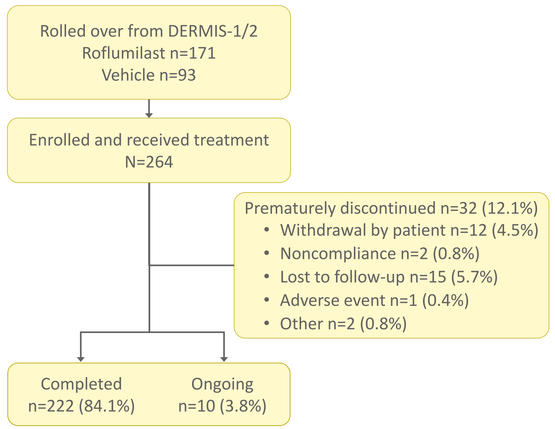
INTRODUCTION

- Various topical treatments are available for chronic plaque psoriasis, such as corticosteroids and vitamin D derivatives; however, there remains an unmet need for effective therapies that are also safe and well-tolerated for long-term use
- 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 phase 2 randomized, vehicle-controlled studies[2,3] and 2 identical, randomized, vehicle-controlled phase 3 trials,[4] the primary endpoint was met, and statistically significant differences in favor of roflumilast were observed for multiple secondary endpoints
  - A 52-week, open-label safety study from the phase 2 study demonstrated maintenance of efficacy and that adverse events (AEs) were similar to the phase 2 study[5]

METHODS

- A phase 3, 24-week, open-label safety study (DERMIS-OLE; NCT04286607) is being conducted in patients ≥2 years of age with psoriasis who successfully completed a prior roflumilast cream study (Cohort 1) and patients ≥2–17 years of age naïve to roflumilast/vehicle (Cohort 2)
- This presentation provides interim results from Cohort 1 as of December 2020, comprising 264 patients from the 2, 8-week phase 3 DERMIS trials who received either roflumilast or vehicle

Figure 1. Disposition of Patients in Cohort 1



RESULTS

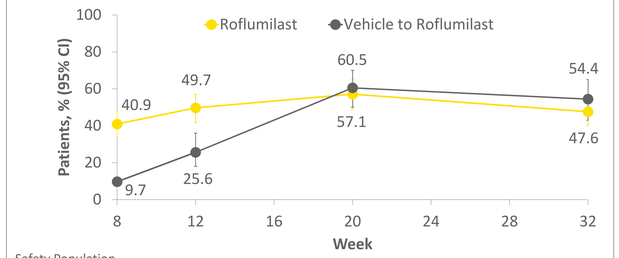
- The completion rate was 84.1%, with 12.1% prematurely discontinuing and an additional 3.8% of patients ongoing at time of the interim analysis (**Figure 1**)
- Long-term exposure to roflumilast did not change the AE profile established by the 52-week, phase 2 long-term safety study as well as the 2 identical, randomized, vehicle-controlled phase 3 studies (**Table 1**)
- Most AEs were mild or moderate in severity
  - One AE was considered likely treatment-related and 3 were possibly related; of note, none of the serious AEs were deemed related to the investigational product
  - AEs considered possibly or likely related to treatment were diarrhea (2 patients), application-site pain (1 patient), and psoriasis (1 patient)
  - Only 1 (0.4%) patient discontinued due to an AE (mild application-site irritation)
  - Depression and weight loss are not risks associated with roflumilast cream 0.3% based on evaluation of the Patient Health Questionnaire depression scale, Modified Patient Health Questionnaire-9 for Adolescents, Children's Depression Inventory 2, Columbia-Suicide Severity Rating Scale, and body weight
- Over the course of the study, ≥96.3% of patients had no evidence of irritation at the application sites as assessed by investigators
- Efficacy endpoints of Investigator Global Assessment (IGA) Clear or Almost Clear (**Figure 2**), Intertriginous-Investigator Global Assessment (I-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 (**Figure 5**) were maintained with roflumilast cream for up to 32 weeks

Table 1. Adverse Events

n (%)	Roflumilast Cream (n=171)	Vehicle→ Roflumilast Cream (n=93)	Total (N=264)
Patients with ≥1 TEAE	39 (22.8)	30 (32.3)	69 (26.1)
Patients with TEAE leading to discontinuation	1 (0.6)	0	1 (0.4)
Patients with an SAE	1 (0.6)	2 (2.2)	3 (1.1)
Most common TEAE (>1% total), preferred term			
Sinusitis	3 (1.8)	4 (4.3)	7 (2.7)
Diarrhea	2 (1.2)	4 (4.3)	6 (2.3)
COVID-19	3 (1.8)	2 (2.2)	5 (1.9)
Headache	0	5 (5.4)	5 (1.9)
Anemia	2 (1.2)	1 (1.1)	3 (1.1)
Nausea	0	3 (3.2)	3 (1.1)
Decreased appetite	1 (0.6)	2 (2.2)	3 (1.1)
Back pain	2 (1.2)	1 (1.1)	3 (1.1)
Nephrolithiasis	1 (0.6)	2 (2.2)	3 (1.1)
Hypertension	3 (1.8)	0	3 (1.1)

This table uses the last observation before the first dose of roflumilast cream 0.3% in this open-label safety study.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

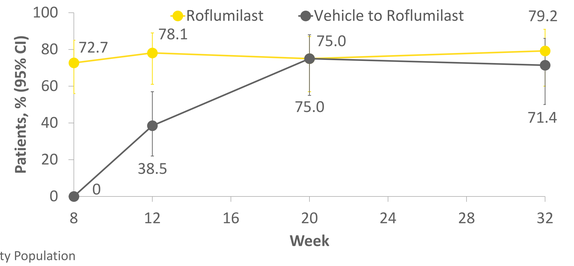
Figure 2. IGA Clear or Almost Clear



Safety Population

Roflumilast	n=171	n=163	n=156	n=145
V→R	n=93	n=86	n=86	n=79

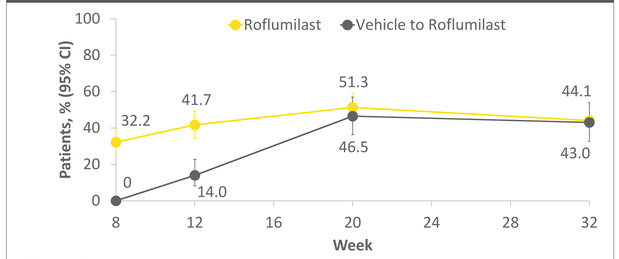
Figure 3. I-IGA Success[a]



Safety Population

Roflumilast	n=33	n=32	n=28	n=24
V→R	n=26	n=26	n=24	n=21

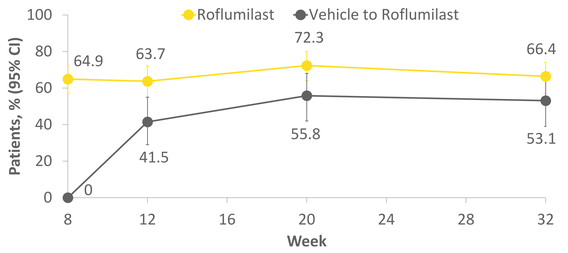
Figure 4. PASI-75



Safety Population

Roflumilast	n=171	n=163	n=156	n=145
V→R	n=93	n=86	n=86	n=79

Figure 5. WI-NRS Success[b]



Safety Population

Roflumilast	n=134	n=124	n=119	n=116
V→R	n=59	n=53	n=52	n=49

[a]I-IGA Success = I-IGA score of Clear or Almost Clear plus ≥2-grade improvement; [b]WI-NRS Success = Achievement of ≥4-point improvement among patients with baseline score ≥4.
Baseline is defined as the last observation recorded prior to the first dose of roflumilast cream 0.3% recorded on Day 1 of parent study or this study (for patients who received vehicle in the parent study).
CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: Intertriginous Investigator Global Assessment; PASI-75: 75% reduction in Psoriasis Area Severity Index score; V→R: vehicle to roflumilast; WI-NRS: Worst Itch Numeric Rating Scale.

CONCLUSIONS

- In this open-label safety study of patients who successfully completed an 8-week, phase 3, vehicle-controlled trial of roflumilast for the treatment of psoriasis
  - Long-term exposure to roflumilast cream 0.3% did not change the safety profile established by the previous studies
  - The local tolerability of roflumilast cream 0.3% was favorable and remained consistent with that of previous studies
- Roflumilast treatment effectively maintained the efficacy demonstrated in the phase 3 DERMIS trials, including maintaining Clear/Almost Clear skin and reduction of itch

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DISCLOSURES

KAP, **DNA**, **MJG**, **LJG**, **ML**, **AYM**, and **DMP** are investigators and/or consultants 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.