Efficacy and Safety of Once-Daily Roflumilast Cream 0.3% in Patients With Knee/Elbow Involvement: Pooled Results From Phase 3 Trials (DERMIS-1 and DERMIS-2)

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INTRODUCTION

- Plaque psoriasis can affect any area of the skin, with knees and elbows being the most common
- Psoriatic plaques on the knees and elbows can be challenging to treat due to thicker stratum corneum in these areas, which impedes topical absorption of medications
- 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 and rapid improvement of psoriasis[2]

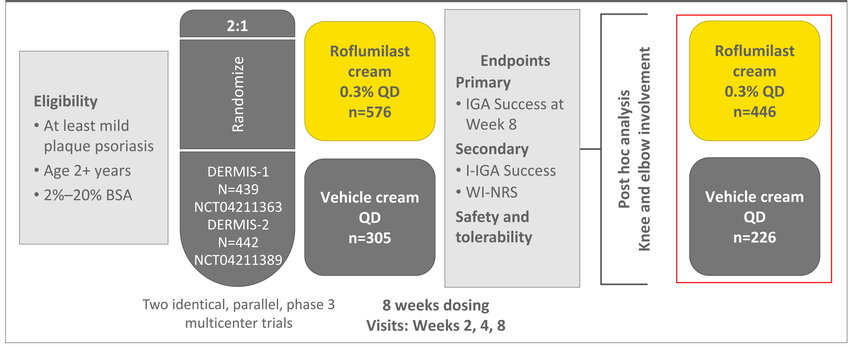
METHODS

- Two identical, phase 3, randomized, double-blind, vehicle-controlled trials (DERMIS-1 and DERMIS-2) were conducted in patients with plaque psoriasis (Figure 1)[3]
- We conducted a post hoc analysis of pooled results from DERMIS-1 and DERMIS-2 to evaluate the subgroup of patients with knee and/or elbow involvement

RESULTS

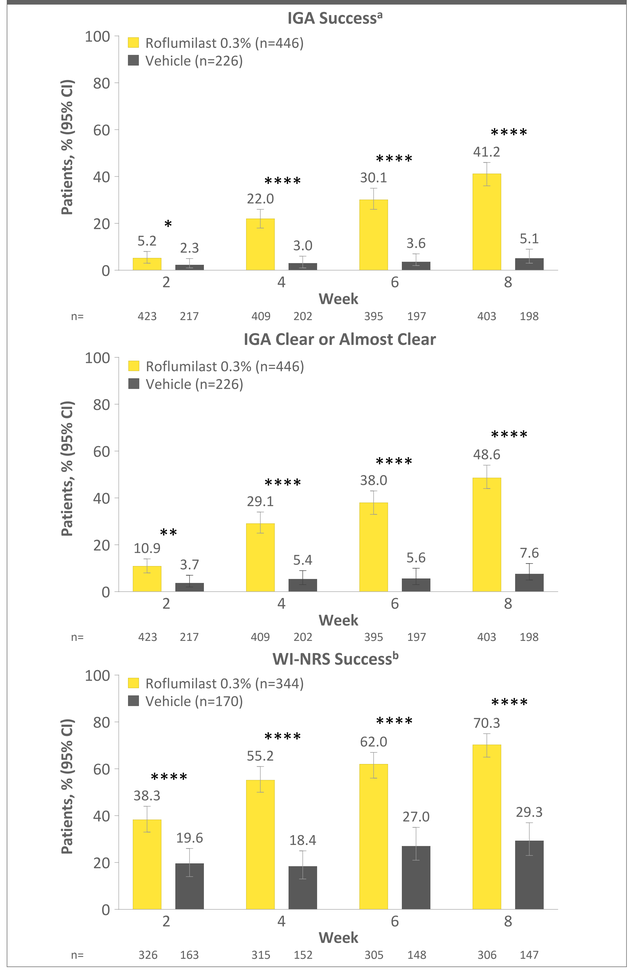
- Significantly more roflumilast-treated patients with knee/elbow involvement achieved Investigator Global Assessment (IGA) Success, IGA status of Clear or Almost Clear, and Worst Itch Numeric Rating Scale (WI-NRS) success versus vehicle at all timepoints (Figure 2)
- Safety and tolerability of roflumilast were similar to that of vehicle in the overall pooled DERMIS analysis (Table 1)
  - Roflumilast cream demonstrated low rates of application-site adverse events (AEs), treatment-related AEs, and discontinuations due to AEs, comparable with vehicle
  - There were no treatment-related serious AEs
  - Local tolerability was highly favorable on the patient and investigator assessments of irritation, burning, and stinging

Figure 1. Study Design



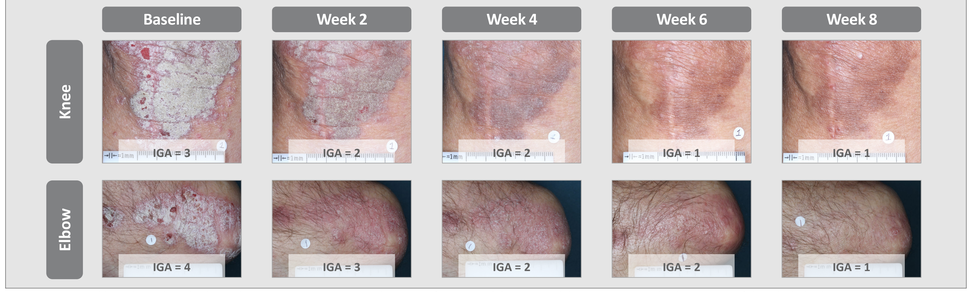
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous-IGA; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 2. IGA Success, IGA Clear or Almost Clear, and WI-NRS Success Versus Vehicle in Patients With Knee/Elbow Involvement



*P<0.05, **P<0.01, ***P<0.001; ****P<0.0001.
[a]IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline. [b]WI-NRS Success = 4-point reduction in score; evaluated in patients with baseline WI-NRS score ≥4.
CI: confidence interval; IGA: Investigator Global Assessment; WI-NRS: Worst Itch Numeric Rating Scale.

Figure 3. Representative Photos of Patients Treated With Roflumilast Cream 0.3% Over Time in DERMIS-1 and DERMIS-2



IGA was measured based on whole body involvement using a 5-point scale ranging from none (0) to severe (4). Images shown display an area of the whole-body measurement.
IGA: Investigator Global Assessment.

Table 1. Overall Pooled DERMIS-1 and DERMIS-2 Summary of AEs

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

- In patients enrolled in the DERMIS-1 or DERMIS-2 clinical trials with psoriatic plaques on their knees and/or elbows, once-daily roflumilast cream demonstrated clinically meaningful efficacy based on IGA Success at the primary endpoint of 8 weeks
- Roflumilast cream significantly improved itch as early as 2 weeks (the earliest timepoint measured)
- Roflumilast cream was well-tolerated with low rates of application-site AEs, treatment-emergent AEs, serious AEs, and discontinuations due to AEs
- The DERMIS phase 3 trials 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, including in patients with difficult-to-treat knee/elbow involvement

DISCLOSURES

LKF, **ZDD**, **AAH**, **CWL**, **DMP**, **KAP**, and **PSY** 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.

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