Roflumilast Cream 0.3% in Patients With Psoriasis: Improvement in Patient-Reported Outcomes and Pruritus From Two Pooled Phase 3 Trials (DERMIS-1/DERMIS-2)

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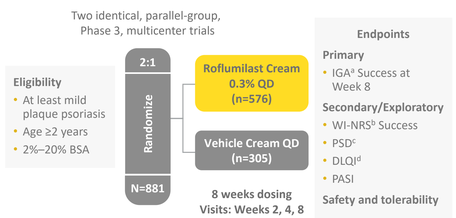
INTRODUCTION

- Chronic plaque psoriasis is an inflammatory skin condition that is a significant source of morbidity, affecting patient emotional health, sleep, and work performance
  - Psoriasis-associated symptoms, such as pain, burning, and itching, impact patient's health-related quality of life
  - In a survey of 3806 patients with psoriasis, >50% of patients reported psoriasis had a least a moderate effect on their quality of life[1]
    - In that survey, ~25% of patients were not receiving treatment[1]
- Roflumilast is a potent phosphodiesterase 4 (PDE4) inhibitor formulated as a water-based cream and foam
  - Roflumilast potency is ~25- to >300-fold higher than apremilast and crisaborole, with roflumilast more closely mimicking cyclic adenosine monophosphate (cAMP) binding to PDE4[2,3]
  - Formulations do not contain ethanol, propylene glycol, or fragrances that can irritate skin
- Efficacy, safety, and tolerability of roflumilast cream in patients with psoriasis have been demonstrated in a Phase 2b study[4] and the individual Phase 3 DERMIS-1 and DERMIS-2 trials[5]
- Here, we report the pooled results for patient-reported outcomes from DERMIS-1 and DERMIS-2

METHODS

- DERMIS-1 (NCT04211363) and DERMIS-2 (NCT04211389) were identical, Phase 3, randomized, double-blind, vehicle-controlled, 8-week studies of once-daily roflumilast cream 0.3% enrolling patients (≥2 years of age) with psoriasis (body surface area 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
  - Patient-reported outcomes included Worst Itch Numeric Rating Scale (WI-NRS; Success: ≥4-point improvement in patients with baseline score ≥4), Psoriasis Symptom Diary (PSD), and Dermatology Life Quality Index (DLQI)
  - Safety and tolerability were also assessed

Figure 1. Study Design



IGA Success = IGA of Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
[a]A 5-point scale ranging from 0 (clear) to 4 (severe). [b]An 11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable) over the preceding 24 hours. [c]A 16-item assessment on a scale from 0 to 10, with higher scores indicating greater severity or burden. [d]A 10-item questionnaire answered on 4-point scales (range: 0 [not at all/not relevant] to 3 [very much]).
BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; PASI: Psoriasis Area Severity Index; PSD: Psoriasis Symptom Diary; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale.

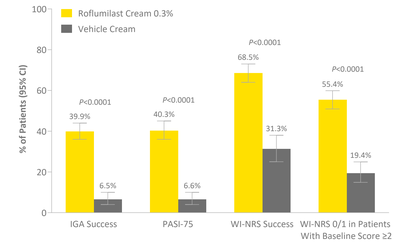
RESULTS

- Demographics and baseline characteristics were similar in the treatment groups (**Table 1**)
- Significantly more roflumilast-treated patients achieved IGA Success at Week 8 than vehicle-treated patients (39.9% vs 6.5%; *P*<0.0001; **Figure 2**)
- Greater improvement in pruritus was observed in roflumilast-treated patients than in vehicle-treated patients at Week 8 (WI-NRS Success: 68.5% vs 31.3%; WI-NRS score 0/1: 55.4% vs 19.4%; both *P*<0.0001; **Figure 2**)
  - Differences in itch were observed at the earliest time point evaluated (Week 2)

Table 1. Pooled Baseline Demographics and Disease Characteristics

	Roflumilast Cream 0.3% (n=576)	Vehicle Cream (n=305)
Age, 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)
>1 race	3 (0.5)	1 (0.3)
IGA, 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)
WI-NRS, mean (SD)	5.7 (2.7)	5.9 (2.8)
Total PSD, mean (SD)	70.5 (41.6)	74.8 (41.2)
DLQI, mean (SD)	7.1 (5.6)	7.4 (5.4)

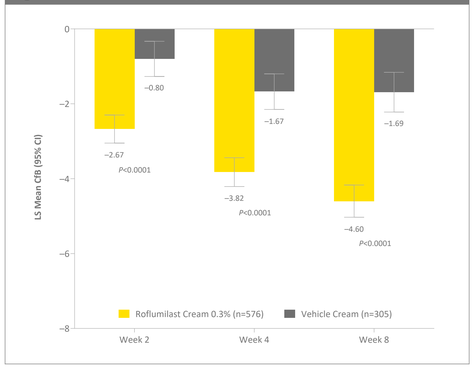
Figure 2. Pooled DERMIS Results at Week 8



Evaluated in the intent-to-treat population.
PASI-75 = 75% reduction in PASI. CI: confidence interval.

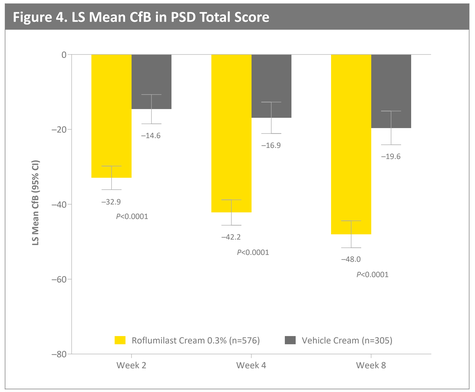
- Also at Week 8, roflumilast-treated patients had greater reduction from baseline in DLQI total score (−4.6 vs −1.69; *P*<0.0001; **Figure 3**) and mean change from baseline in PSD total score (−69.2% vs −26.0%; *P*<0.0001; **Figure 4**) compared with patients treated with vehicle
- Consistent improvement occurred across PSD domains of patient-reported signs and symptoms of their psoriasis (severity and bothersomeness; **Figures 5A, 5B**), as well as improvement in emotional domains (embarrassment; **Figure 5C**)

Figure 3. LS Mean CfB in DLQI Total Score



From an analysis of covariance model with study, randomized baseline IGA, and baseline intertriginous involvement as factors and corresponding baseline as a covariate. DLQI score is the sum of 10 questions rated concerning the patient's perception of the impact of skin disease on different aspects of their health-related quality of life over the last week. It ranges from 0 to 30, where higher scores indicate the most impact on the patient's health-related quality of life.
CfB: change from baseline; CI: confidence interval; LS: least squares.

Figure 4. LS Mean CfB in PSD Total Score



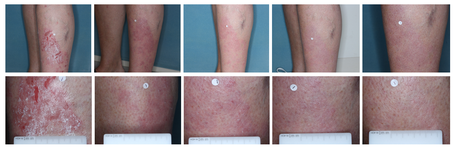
If ≥1 item is missing, the score is not calculated. Estimates for LS means (change/percent change from baseline and difference from vehicle [ie, change/percent change from baseline for roflumilast cream 0.3% minus change from baseline for vehicle cream]) and accompanying 95% CIs, and *P* values are from an analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline PSD score as independent variables. Baseline is the last non-missing measurement taken before the first application of study drug. CfB is calculated as result − baseline result.
CfB: change from baseline; CI: confidence interval; LS: least squares.

Figure 5. Individual PSD Questions at Week 8

If ≥1 item is missing, the score is not calculated. Estimates for LS means (change/percent change from baseline and difference from vehicle [ie, change/percent change from baseline for roflumilast cream 0.3% minus change from baseline for vehicle cream]) and accompanying 95% CIs, and *P* values are from an analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline PSD score as independent variables. Baseline is the last non-missing measurement taken before the first application of study drug. CfB is calculated as result − baseline result.
CfB: change from baseline; CI: confidence interval; LS: least squares.

- A series of photographs of a patient with improvement in psoriasis following roflumilast treatment is shown in **Figure 6**

Figure 6. Improvement in Psoriasis in a Patient Treated With Roflumilast Cream 0.3% QD



- Roflumilast cream was associated with low rates of application site adverse events (AEs), treatment-related AEs, and discontinuations due to AEs (**Table 2**)
  - These rates were comparable with vehicle
- ≥97.7% of patients in each group had no signs of irritation on investigator-rated local tolerability assessments at any time point
- ≥99.4% of patients treated with roflumilast cream 0.3% and ≥98.8% of patients treated with vehicle reported no or mild sensation after applying roflumilast cream at any time point

Table 2. Overall AEs

n (%)	Roflumilast Cream 0.3% (n=576)	Vehicle Cream (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.

CONCLUSION

- Clinically meaningful improvement in disease burden occurred by Week 2, the first time point at which the patient-reported outcomes of WI-NRS, PSD, and DLQI were assessed
- Treatment with once-daily roflumilast cream resulted in improvement in patient quality of life, emotional wellbeing, and signs and symptoms of psoriasis

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DISCLOSURES

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