Effects of Roflumilast Cream on Patient Burden and Work Productivity in Patients With Psoriasis

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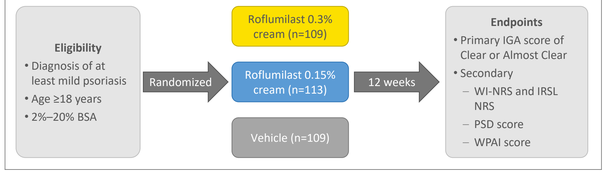
INTRODUCTION

- Chronic plaque psoriasis is an inflammatory skin condition that is a significant source of morbidity, affecting patient's emotional health, sleep, and work performance
  - Psoriasis-associated symptoms, such as pain, burning, and itching, impact patients' health-related quality of life[1]
- Indirect costs associated with psoriasis are estimated at more than $16 billion annually, with absenteeism and presenteeism contributing approximately equally and accounting for up to 40% of the costs[2]
- Current topical treatment options include corticosteroids, vitamin D analogues, and tazarotene[3]
  - Topical corticosteroids cannot be used long-term due to side effects and limitations on facial or intertriginous application
  - Although they may be used long-term, vitamin D analogues and tazarotene may cause irritation and often have lower efficacy with a slower onset of action
- 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[4]
- 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, once-daily treatment with roflumilast cream 0.3% or 0.15% resulted in significant and rapid improvement of psoriasis[5]
  - This poster presents efficacy and safety results of roflumilast cream 0.3% and 0.15% from that phase 2b trial, including effects on patient burden

METHODS

- In this randomized, double-blind, phase 2b trial of 331 adults with chronic plaque psoriasis, patients were randomized to once-daily roflumilast 0.3% (n=109), roflumilast 0.15% (n=113), or vehicle (n=109) for 12 weeks (ClinicalTrials.gov identifier: NCT03638258; **Figure 1**)
- Inclusion criteria were psoriasis of at least mild severity (score ≥2 on the 5-point Investigator's Global Assessment [IGA]) and a score of ≥2 on a modified version of the Psoriasis Area and Severity Index (PASI-high discrimination; range: 0, no disease; 72, maximal disease)[6]
- The primary endpoint was the percentage of patients achieving IGA status of Clear or Almost Clear at Week 6
  - Secondary and exploratory endpoints included Worst Itch Numeric Rating Scale (WI-NRS), Itch-related Sleep Loss (IRSL) NRS scores, Psoriasis Symptom Diary (PSD), and Work Productivity and Activity Impairment (WPAI)
  - Patients rated itching severity on the WI-NRS (scale: 0 [no itching] to 10 [worst itch imaginable]),[1] IRSL (scale: 0 [no sleep loss] to 10 [sleep loss as bad as it could be]) and Fatigue NRS (scale: 0 [no fatigue] to 10 [fatigue as bad as it could be]) over the previous 24 hours
  - Patients used the PSD to determine the severity and impact of psoriasis-related signs and symptoms over the past 24 hours
    - Patients rated each variable in the 16-item assessment on a scale from 0 to 10, with higher scores indicating greater severity or burden[7]
  - Patients reported the impact of psoriasis on their ability to work and perform daily activities over the past 7 days on the WPAI questionnaire

Figure 1. Study Design

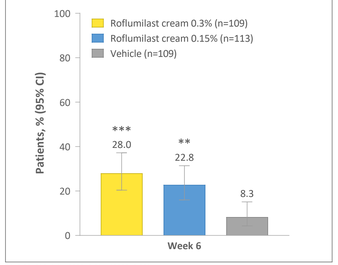


BSA: body surface area; IGA: Investigator's Global Assessment; IRSL: Itch-related Sleep Loss; NRS: Numeric Rating Scale; PSD: Psoriasis Symptom Diary; WI-NRS: Worst Itch Numeric Rating Scale; WPAI: Work Productivity and Activity Impairment.

RESULTS

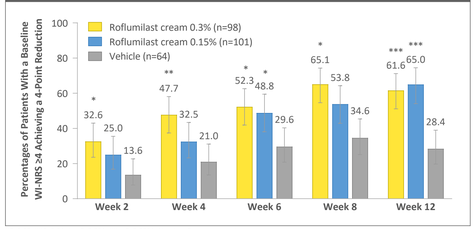
- More patients treated with roflumilast cream 0.3% (P<0.001 vs vehicle) and roflumilast cream 0.15% (P=0.004 vs vehicle) than patients treated with vehicle cream met the primary endpoint (**Figure 2**)[4]
- Among patients with baseline WI-NRS ≥4, more patients treated with roflumilast 0.3% achieved ≥4-point improvement on the WI-NRS (**Figure 3**)
  - Differences were seen as early as Week 2, the first timepoint evaluated
- Roflumilast-treated patients had improvement in IRSL beginning at Week 6 (P≤0.022; **Figure 4**)
- The Fatigue NRS score improved over time for all 3 treatment groups; the mean decrease from baseline to Week 12 was 1.6 with roflumilast 0.3% (P=0.05 vs vehicle), 1.1 with roflumilast 0.15%, and 1.0 with vehicle
- Roflumilast also resulted in sustained improvements in the total PSD score (**Figure 5**) and individual PSD domains (**Table 1**)
  - Both roflumilast-treated groups showed improvements in patient severity and burden of scaling by Week 2 (the first timepoint analyzed); stinging and skin cracking by Week 4; and burning and pain by Week 6
- In a post hoc analysis, roflumilast-treated patients had an improvement in the WPAI assessments of impairment while working by Week 2 and general activity impairment outside of work and overall work impairment by Week 12 (**Figure 6**)
- Most (97%) adverse events (AEs) were mild to moderate in severity, and rates were similar across all treatment groups (**Table 2**)
  - More patients in the vehicle group discontinued therapy due to AEs
  - Rates of application-site pain were low and comparable with that of the vehicle

Figure 2. Patients Achieving IGA Status of Clear or Almost Clear at Week 6 (Primary Endpoint)



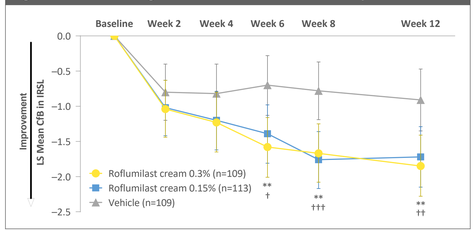
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001.
Data are presented for intent-to-treat population. CI: confidence interval; IGA: Investigator's Global Assessment.

Figure 3. Percentage of Patients With a Worst Itch Numeric Rating Scale ≥4 at Baseline Achieving a 4-Point Reduction



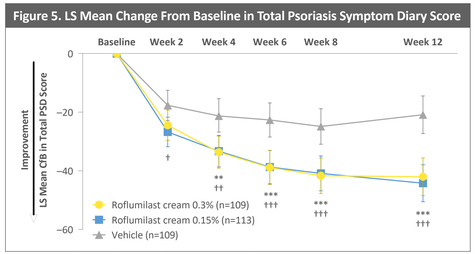
*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. Nominal P-values vs vehicle.
Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. WI-NRS: Worst Itch Numeric Rating Scale.

Figure 4. LS Mean Change From Baseline in Itch-Related Sleep Loss Score



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001 Roflumilast 0.3% cream vs vehicle.
†P<0.05; ††P<0.01; †††P<0.001; ††††P<0.0001 Roflumilast 0.15% cream vs vehicle.
CfB: change from baseline; IRSL: Itch-related Sleep Loss; LS: least squares

Figure 5. LS Mean Change From Baseline in Total Psoriasis Symptom Diary Score



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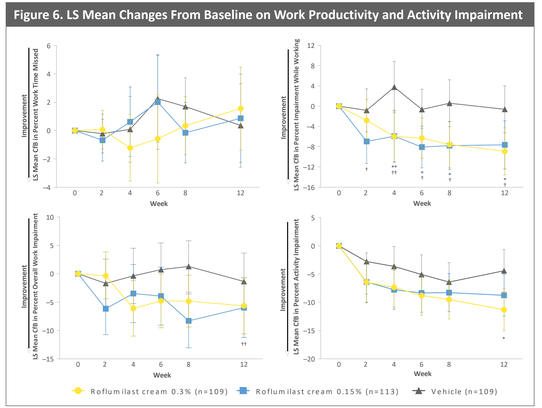
†P<0.05; ††P<0.01; †††P<0.001; ††††P<0.0001 Roflumilast 0.15% cream vs vehicle.
Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward when linear interpolation was not computationally possible. CfB: change from baseline; LS: least squares; PSD: Psoriasis Symptom Diary.

Table 1. Individual Domains on the Psoriasis Symptom Diary

	Roflumilast 0.3% Cream (n=109)		Roflumilast 0.15% Cream (n=113)	
	Week 2	*Week 12*	*Week 2*	*Week 12*
How *severe* was your psoriasis-related …				
Itching in the past 24 hours?				
Stinging in the past 24 hours?				
Burning in the past 24 hours?				
Skin cracking in the past 24 hours?				
Pain in the past 24 hours?				
Scaling in the past 24 hours?				
How *bothered* were you by your psoriasis-related …				
Itching in the past 24 hours?				
Stinging in the past 24 hours?				
Burning in the past 24 hours?				
Skin cracking in the past 24 hours?				
Pain in the past 24 hours?				
Scaling in the past 24 hours?				
Noticeable color of psoriasis in the past 24 hours?				
Hiding psoriasis in the past 24 hours?				
Avoiding activities in the past 24 hours?				
Embarrassed by psoriasis in the past 24 hours?				

Yellow boxes indicate nominal P-values vs vehicle <0.05. Gray and white boxes are not significant vs vehicle. Vehicle n=107. Analyses were conducted on the intent-to-treat population. Missing data were imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible.

Figure 6. LS Mean Changes From Baseline on Work Productivity and Activity Impairment



*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001 Roflumilast 0.3% cream vs vehicle.
†P<0.05; ††P<0.01; †††P<0.001; ††††P<0.0001 Roflumilast 0.15% cream vs vehicle.
Data are presented for intent-to-treat population. Missing data imputed using linear interpolation and last observation carried forward where linear interpolation was not computationally possible. CfB: change from baseline; LS: least squares.

Table 2. Summary of AEs

TEAE, n (%)	Roflumilast 0.3% Cream (n=109)	Roflumilast 0.15% Cream (n=110)	Vehicle (n=107)
Patients with any TEAE	42 (38.5)	30 (27.3)	32 (29.9)
Patients with any treatment-related TEAE	7 (6.4)	3 (2.7)	7 (6.5)
Patients with any SAE[a]	1 (0.9)	1 (0.9)	2 (1.9)
Patients who discontinued study due to AE[b]	1 (0.9)	0	2 (1.9)
Most common TEAE (>2% of patients in any group)			
Upper respiratory tract infection (including viral)	9 (8.3)	8 (7.3)	4 (3.7)
Nasopharyngitis	4 (3.7)	3 (2.7)	4 (3.7)
Application-site pain	2 (1.8)	1 (0.9)	3 (2.8)
Sinusitis	3 (2.8)	0	0
Urinary tract infection	0	3 (2.7)	1 (0.9)

Data are presented for safety population. [a]Roflumilast 0.3%: worsening of chest pain in a patient with history of myocardial infarction; roflumilast 0.15%: melanoma (not in treatment area); vehicle group: acute infarction of left basal ganglia, spontaneous miscarriage. [b]Roflumilast 0.3%: onset of worsening psoriasis; vehicle: mood swings, contact dermatitis. AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Roflumilast cream 0.3% and 0.15% demonstrated improvements in psoriasis across efficacy measures
  - Roflumilast significantly increased the percentage of patients with IGA Clear or Almost Clear
  - Roflumilast cream 0.3% improved itch and IRSL as early as 2 weeks, the first timepoint measured
  - Once-daily treatment with roflumilast cream 0.3% and 0.15% improved total score and individual domains of the PSD
  - At Week 12, roflumilast-treated patients had greater improvement of fatigue, impairment while working, overall work impairment, and general activity impairment
- Roflumilast cream was well-tolerated with low rates of treatment-related AEs, serious AEs, and discontinuations due to AEs
  - Rates of application-site pain were low and similar across all groups

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DISCLOSURES

LHK, **LA**, **LKF**, **MJG**, **HCH**, **SEK**, **MGL**, **VM**, **LO**, **SS**, and **LSG** 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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