Efficacy and Safety of Roflumilast Cream 0.3% in Patients With Chronic Plaque Psoriasis: Pooled PASI and PASI-HD Results From the DERMIS-1 and DERMIS-2 Phase 3 Trials

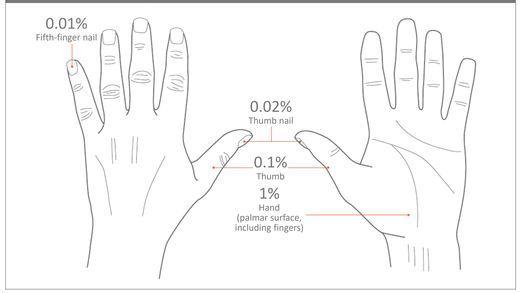
Kim A. Papp,[1] Mark G. Lebwohl,[2] H. Chih-ho Hong,[3] Leon H. Kircik,[2,4] David M. Pariser,[5] Bruce Strober,[6] Gerald Krueger,[7] David Krupa,[8] Patrick Burnett,[8] David Berk,[8] Robert Higham[8]

[1]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Department of Dermatology and Skin Science, University of British Columbia and Probity Medical Research, Surrey, BC, Canada; [4]Indiana Medical Center, Indianapolis, IN, Physicians Skin Care, PLLC, and Skin Sciences, PLLC, Louisville, KY, USA; [5]Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; [6]Yale University School of Medicine, New Haven, CT, and Central Connecticut Dermatology, Cromwell, CT, USA; [7]University of Utah Health, Salt Lake City, UT, USA; [8]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

INTRODUCTION

- The Psoriasis Area and Severity Index (PASI) is used to assess disease severity of plaque psoriasis in clinical trials[1]
  - The PASI is not precise when the regional area of involvement is <10% of the body surface area (BSA) of a specific anatomical region[2]
  - A modified version of the PASI, termed PASI-high discrimination (PASI-HD), allows more precise assessment of psoriasis severity in body regions where <10% of the BSA is affected (Figure 1)[2]
- Topical roflumilast cream 0.3% is a selective, potent, phosphodiesterase 4 inhibitor that was recently approved for once-daily treatment of psoriasis
- In this poster, we describe pooled results from 2 phase 3 clinical trials (DERMIS-1 and DERMIS-2) evaluating the efficacy and safety of once-daily topical roflumilast in patients (≥2 years) with psoriasis involving 2–20% BSA, including changes in PASI and PASI-HD

Figure 1. Hand Locations for Estimating Area of Psoriasis Involvement When <10% for Determining PASI-HD[2]

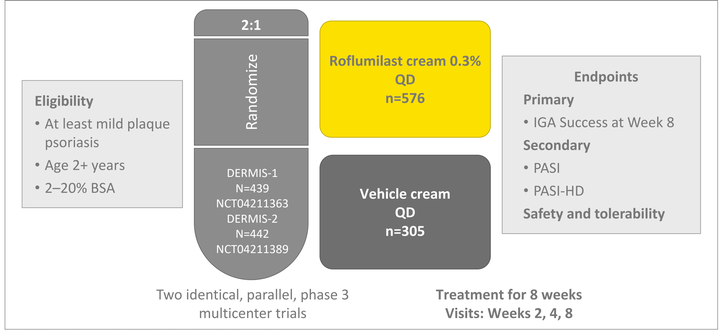


Papp KA, et al. The proposed PASI-HD provides more precise assessment of plaque psoriasis severity in anatomical regions with a low area score. *Dermatol Ther (Heidelb)*. 2021;11(4):1079-1083; reproduced with permission from SNCSC.[2]
PASI-HD: Psoriasis Area and Severity Index-high discrimination.

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 2)
- 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
  - PASI and PASI-HD scores were evaluated as secondary endpoints

Figure 2. Study Design



IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline.
BSA: body surface area; IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; PASI-HD: PASI-high discrimination; QD: once daily.

RESULTS

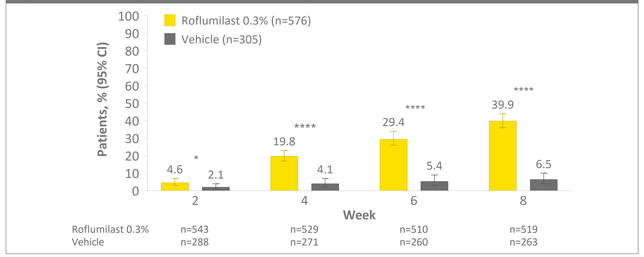
- Demographics and baseline characteristics were similar in the treatment groups (Table 1)
- Overall, significantly more roflumilast-treated patients than vehicle-treated patients achieved IGA Success (39.9% vs 6.5%; *P*<0.0001) at Week 8 (Figure 3)
  - Significantly greater percentages of patients in the roflumilast group had IGA Success at other timepoints compared with that of the vehicle group
- Statistically significant differences favoring roflumilast were observed at Week 8 for percentages of patients achieving 50% reduction in PASI (72.1% vs 25.5%; *P*<0.0001) and PASI-HD (79.4% vs 33.1%, respectively; *P*<0.0001; Figure 4A)
  - Similar results were observed for percentages of patients achieving 75% reduction (Week 8: 40.3% vs 6.5% and 59.9% vs 17.9%, respectively; *P*<0.0001; Figure 4B) and percentages of patients achieving 90% reduction (Week 8: 19.7% vs 2.3% and 39.9% vs 9.1%, respectively; *P*<0.0001; Figure 4C)
- For the percentages of patients achieving 100% reduction in PASI and PASI-HD, significantly more roflumilast- than vehicle-treated patients achieved this endpoint (Week 8: 12.3% vs 0.8% for both; *P*<0.001; Figure 4D) and rates for PASI and PASI-HD were identical at each timepoint
  - The PASI-HD provided higher discrimination of effects of treatment in areas with <10% of the BSA affected than the traditional PASI

Table 1. Pooled Baseline Demographics and Disease Characteristics

	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
Age in years, mean (SD)	47.2 (14.6)	47.9 (15.0)
Sex		
Male, n (%)	365 (63.4)	196 (64.3)
Female, n (%)	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)
PASI, mean score (SD)	6.4 (3.2)	6.9 (3.6)

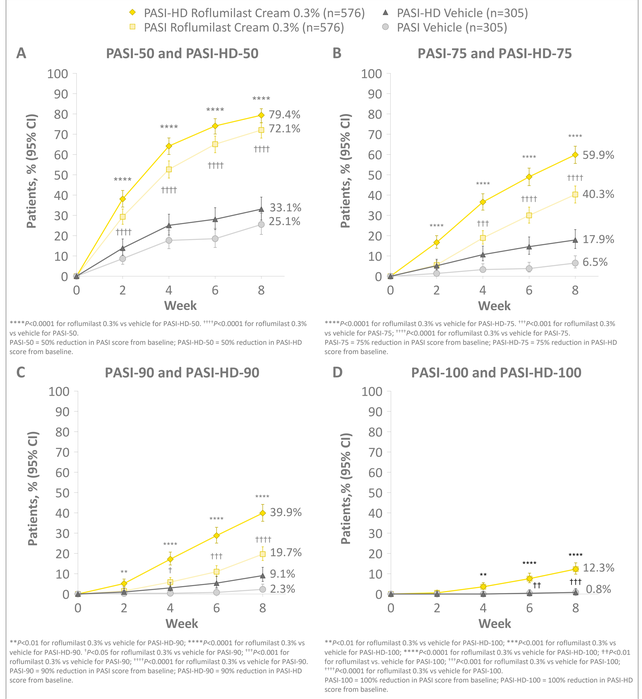
BSA: body surface area; IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; SD: standard deviation.

Figure 3. Percentages of Patients Achieving IGA Success 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.
CI: confidence interval; IGA: Investigator Global Assessment.

Figure 4. Percentages of Patients Achieving (A) PASI-50 and PASI-HD-50, (B) PASI-75 and PASI-HD-75, (C) PASI-90 and PASI-HD-90, and (D) PASI-100 and PASI-HD-100



****P<0.0001 for roflumilast 0.3% vs vehicle for PASI-HD-50. ††††P<0.0001 for roflumilast 0.3% vs vehicle for PASI-50.
PASI-50 = 50% reduction in PASI score from baseline; PASI-HD-50 = 50% reduction in PASI-HD score from baseline.

****P<0.0001 for roflumilast 0.3% vs vehicle for PASI-HD-75. †††P<0.001 for roflumilast 0.3% vs vehicle for PASI-75; ††††P<0.0001 for roflumilast 0.3% vs vehicle for PASI-75.
PASI-75 = 75% reduction in PASI score from baseline; PASI-HD-75 = 75% reduction in PASI-HD score from baseline.

**P<0.01 for roflumilast 0.3% vs vehicle for PASI-HD-90; ****P<0.0001 for roflumilast 0.3% vs vehicle for PASI-HD-90. †P<0.05 for roflumilast 0.3% vs vehicle for PASI-90; †††P<0.001 for roflumilast 0.3% vs vehicle for PASI-90; ††††P<0.0001 for roflumilast 0.3% vs vehicle for PASI-90.
PASI-90 = 90% reduction in PASI score from baseline; PASI-HD-90 = 90% reduction in PASI-HD score from baseline.

**P<0.01 for roflumilast 0.3% vs vehicle for PASI-HD-100; ***P<0.001 for roflumilast 0.3% vs vehicle for PASI-HD-100; ****P<0.0001 for roflumilast 0.3% vs vehicle for PASI-HD-100; ††P<0.01 for roflumilast vs. vehicle for PASI-100; †††P<0.001 for roflumilast 0.3% vs vehicle for PASI-100; ††††P<0.0001 for roflumilast 0.3% vs vehicle for PASI-100.
PASI-100 = 100% reduction in PASI score from baseline; PASI-HD-100 = 100% reduction in PASI-HD score from baseline.

CI: confidence interval; PASI: Psoriasis Area and Severity Index; PASI-HD: PASI-high discrimination.

Safety

- Roflumilast cream demonstrated low rates of application-site adverse events (AEs), treatment-related AEs, and discontinuations due to AEs, comparable with vehicle (Table 2)
- There were no treatment-related serious AEs
- ≥97.7% of patients in each group had no signs of irritation at Week 4 or Week 8 on investigator-rated local tolerability assessments
- ≥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 treatment at Weeks 4 and 8

Table 2. Overall AEs[3]

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

- The PASI-HD provides higher discrimination of effects of treatment in areas with <10% of the BSA affected than the traditional PASI while maintaining other standard components of the PASI
  - The improved sensitivity of the PASI-HD is demonstrated with increasing differences between the PASI and PASI-HD as the area involved decreases (ie, differences are greater with PASI-90 than PASI-75 and PASI-50)
- Roflumilast cream 0.3% provided clinically meaningful response in >70% of patients
- Roflumilast cream 0.3% provided superior improvement on IGA Success, PASI scores, and PASI-HD scores versus vehicle with favorable safety and local tolerability in patients with psoriasis in 2 phase 3 trials

REFERENCES

1. Fredriksson T, et al. *Dermatologica* 1978;157:238–244.
2. Papp KA, et al. *Dermatol Ther (Heidelb)* 2021;11:1079–1083.
3. Lebwohl MG, et al. Poster presented at: American Academy of Dermatology, March 25–29, 2022, Boston, MA, USA.

ACKNOWLEDGEMENTS

- This study was supported by Arcutis Biotherapeutics, Inc.
- Thank you to the investigators and their staff for their participation in the trials
- We are grateful to the study participants and their families for their time and commitment
- Writing support was provided by Christina McManus, PhD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

KAP, MGL, HCH, LHK, DMP, BS, and **GK** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **DK, PB, DRB,** and **RH** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.