Roflumilast Cream 0.3% in Patients With Chronic Plaque Psoriasis: Individual Patient PASI and PASI-HD Responses: Pooled DERMIS-1 and DERMIS-2 Phase 3 Trials

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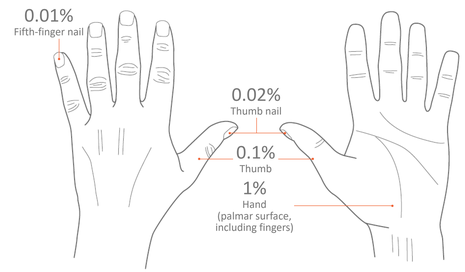
INTRODUCTION

- The Psoriasis Area and Severity Index (PASI) is used to assess disease severity of plaque psoriasis in clinical trials[1]
  - The PASI is less precise when <10% of the area of a specific anatomical region is involved[2]
  - A modified version of the PASI, termed PASI-high discrimination (PASI-HD), generates a linear score when the area of involvement is <10% of the anatomical region; scores of 1–9% become 0.1–0.9 (in place of 1 with PASI)
  - PASI-HD allows more precise assessment of psoriasis severity in body regions where <10% of the area is affected (**Figure 1**)[2]
- Roflumilast cream 0.3% is a highly potent phosphodiesterase 4 inhibitor approved as a nonsteroidal, once-daily treatment for patients with plaque psoriasis
- Pooled efficacy and safety results of two Phase 3 clinical trials (DERMIS-1 and DERMIS-2) in patients aged ≥2 years with plaque psoriasis have been presented previously[3]
- We present individual patient PASI and PASI-HD responses

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

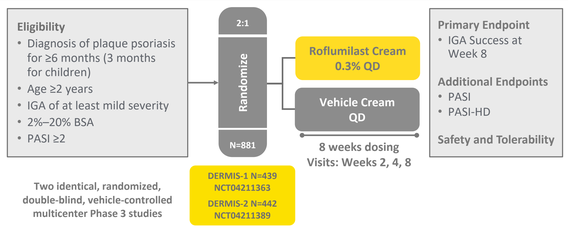


Papp KA, et al. The proposed PASI-HD provides more precise assessment of plaque psoriasis severity in anatomical regions with a low area score. *Dermatol Ther (Heidelb)* 2021;11(4):1079-1083; reproduced with permission from SNCSC.[2]
PASI-HD: Psoriasis Area and Severity Index-high discrimination.

METHODS

- DERMIS-1 and DERMIS-2 were identical, Phase 3, randomized, double-blind, vehicle-controlled, 8-week trials of once-daily roflumilast cream 0.3% in patients (≥2 years of age) with psoriasis (body surface area affected: 2%–20%; **Figure 2**)
- The primary efficacy endpoint was Investigator Global Assessment (IGA) Success (score of Clear or Almost Clear plus ≥2-grade improvement from baseline) at Week 8
  - PASI and PASI-HD scores were evaluated as 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

- Baseline demographics and disease characteristics were similar in roflumilast- and vehicle-treated patients (**Table 1**)

Table 1

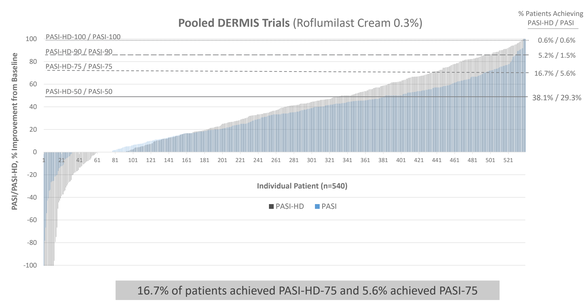
	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
Age in years, mean (SD)	47.2 (14.6)	47.9 (15.0)
Sex, n (%)		
Male	365 (63.4)	196 (64.3)
Female	211 (36.6)	109 (35.7)
IGA score, n (%)		
2 (mild)	101 (17.5)	44 (14.4)
3 (moderate)	426 (74.0)	240 (78.7)
4 (severe)	49 (8.5)	21 (6.9)
PASI, mean score (SD)	6.4 (3.2)	6.9 (3.6)
PASI-HD, mean score (SD)	4.2 (3.8)	4.8 (4.3)

IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; PASI-HD: PASI-high-discrimination; SD: standard deviation.

- At Week 8, statistically significantly more roflumilast- than vehicle-treated patients achieved:
  - IGA Success (39.9% vs 6.5%; *P*<0.0001)[3]
  - IGA of Clear or Almost Clear (48.0% vs 9.5%; nominal *P*<0.0001)[3]
  - Improvements in PASI and PASI-HD
    - 40.3% of roflumilast-treated patients achieved a 75% reduction in PASI at Week 8 compared with 6.5% of vehicle-treated (*P*<0.0001)
    - 59.9% of roflumilast-treated patients achieved a 75% reduction in PASI-HD at Week 8 compared with 17.9% of vehicle-treated (*P*<0.0001)
- A large majority of roflumilast-treated patients experienced some improvement in PASI and PASI-HD (**Figure 3**)

Figure 3A. Individual Patient Improvement in PASI and PASI-HD

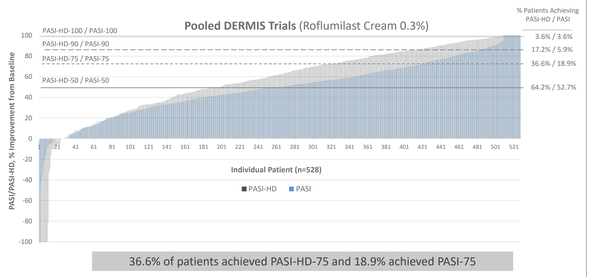
A. Individual Patient Improvement in PASI and PASI-HD at Week 2



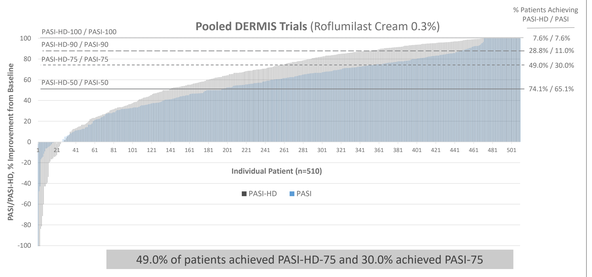
PASI: Psoriasis Area and Severity Index; PASI-50: 50% reduction in PASI score from baseline; PASI-75: 75% reduction in PASI score from baseline; PASI-90: 90% reduction in PASI score from baseline; PASI-100: 100% reduction in PASI score from baseline; PASI-HD: PASI-high discrimination; PASI-HD-50: 50% reduction in PASI-HD score from baseline; PASI-HD-75: 75% reduction in PASI-HD score from baseline; PASI-HD-90: 90% reduction in PASI-HD score from baseline; PASI-HD-100: 100% reduction in PASI-HD score from baseline.

Figure 3. Individual Patient Improvement in PASI and PASI-HD

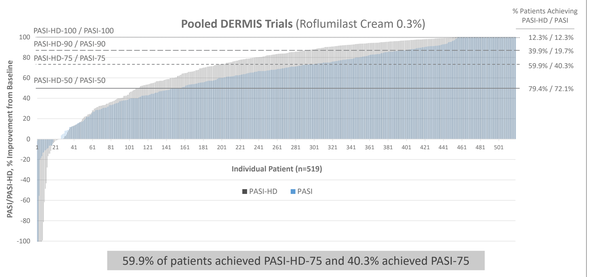
B. Individual Patient Improvement in PASI and PASI-HD at Week 4



C. Individual Patient Improvement in PASI and PASI-HD at Week 6



D. Individual Patient Improvement in PASI and PASI-HD at Week 8



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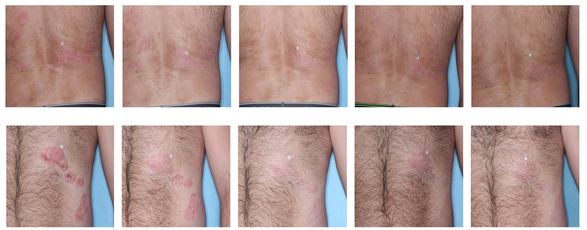
- Patient photographs demonstrating disease improvement over time are shown in **Figure 4**

Figure 4. Changes in Psoriasis in a Patient Treated With Roflumilast Cream 0.3%



BASELINE	WEEK 2	WEEK 4	WEEK 6	WEEK 8
IGA: 3 WI-NRS: 7 PASI: 13.7 PASI-HD: 12.3	IGA: 2 WI-NRS: 8 Improvement in: PASI: 35% PASI-HD: 40%	IGA: 2 WI-NRS: 3 Improvement in: PASI: 45% PASI-HD: 51%	IGA: 2 WI-NRS: 2 Improvement in: PASI: 66% PASI-HD: 87%	IGA: 1 WI-NRS: 3 Improvement in: PASI: 85% PASI-HD: 95%

37-year-old Male, White/Not Hispanic or Latino

IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; PASI-HD: PASI-high discrimination; WI-NRS: Worst Itch-Numeric Rating Scale.

SAFETY

- Roflumilast cream demonstrated low rates of application-site adverse events (AEs), treatment-related AEs, and discontinuations due to AEs, comparable with vehicle
- Approximately 96% of patients reported no or mild sensation after the first application of roflumilast cream 0.3%, improving to more than 99% of patients at Week 4 and Week 8

CONCLUSIONS

- The PASI-HD provides higher discrimination of effects of treatment when the area of involvement is <10% of a given anatomic region 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 greater improvement in IGA Success, IGA of Clear or Almost Clear, and PASI/PASI-HD versus vehicle in patients with psoriasis in two Phase 3 trials
- Safety and tolerability were favorable, with nearly all roflumilast- and vehicle-treated patients reporting no or mild sensation at the application site by Week 8

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.

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DISCLOSURES

JDR, HCH, LHK, MG, MGL, KAP, LSG, and AAH are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; MS, DK, DHC, PB, DRB, and RCH are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.