0462

Efficacy and Tolerability of Roflumilast Cream 0.15% for Atopic Dermatitis: Pooled Subgroup Analysis of Patients With Face/Eyelid Involvement From Phase 3 INTEGUMENT-1/2 Trials

Eric Simpson,[1] Alexandra Golant,[2] Lawrence F. Eichenfield,[3] Amy Paller,[4] Jonathan I. Silverberg,[5] Melinda J. Gooderham,[6,7] Mercedes E. Gonzalez,[8] H. Chih-ho Hong,[7,9] David Krupa,[10] Diane Hanna,[10] Patrick Burnett,[10] David H. Chu,[10] David R. Berk[10]

[1]Oregon Health & Science University, Portland, OR; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Rady Children's Hospital, University of California San Diego School of Medicine, San Diego, CA; [4]Northwestern University Feinberg School of Medicine, Chicago, IL; [5]The George Washington University School of Medicine and Health Sciences, Washington, D.C.; [6]SKIN Centre for Dermatology, Queen's University, Kingston, ON; [7]Probity Medical Research, Surrey, BC; [8]Pediatric Skin Research, Miami, FL; [9]University of British Columbia, Surrey, BC; [10]Arcutis Biotherapeutics, Inc., Westlake Village, CA

ACKNOWLEDGMENTS

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 Kelly M. Fahrbach, PhD, CMPP, and Michele Salemitano, of Ashfield MedComms, an Inizio company, and was funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

ES, AG, LFE, AP, JIS, MJG, MEG, and HCH are investigators and/or consultants for and have received grants/research funding and/or honoraria from Arcutis Biotherapeutics, Inc. DK, DH, PB, DHC, and DRB are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided upon request. This study was funded by Arcutis Biotherapeutics, Inc.

Presented at the 82nd Society for Investigative Dermatology Annual Meeting
May 7–10, 2025; San Diego, CA

INTRODUCTION

- AD is a chronic inflammatory skin disease that commonly affects the face, including the eyelids[1,2]
  - These are high-impact areas for the patient, based on both visibility and sensitivity[2,3]
  - The negative impact of AD with head/face/neck involvement on patient quality of life[4] highlights a need for new, safe treatment options
- There have been advances and approvals in topical treatment options for AD; however, TCS continue to be a mainstay treatment, despite limitations to their use[5]
  - TCS are not approved for long-term use and higher potency TCS are not recommended for use in thin-skinned areas because of an increased risk of cutaneous and systemic AEs[1,5]
- Roflumilast is a phosphodiesterase 4 inhibitor and has been formulated as a topical, water-based cream or foam that does not include fragrances or potential cutaneous irritants[6]
- Roflumilast cream 0.15% was effective and well tolerated in patients with mild-to-moderate AD aged ≥6 years in two phase 3 trials (INTEGUMENT-1/NCT04773587 and INTEGUMENT-2/NCT04773600)[7]
  - Significant improvements, compared to vehicle, were observed across multiple efficacy assessments, including a decrease in itch symptoms (WI-NRS)
  - In July 2024, roflumilast cream 0.15% was approved for patients aged ≥6 years with mild-to-moderate AD[8]
- This analysis assessed roflumilast cream 0.15% efficacy, safety, and application-site tolerability in patients enrolled in the INTEGUMENT-1 and -2 trials with baseline involvement of AD on the face, or specifically on the eyelid(s)

METHODS

Study Design

- INTEGUMENT-1 and INTEGUMENT-2 were phase 3, randomized, double-blind, vehicle-controlled trials that assessed once-daily roflumilast cream 0.15% over 4 weeks in patients aged ≥6 years with mild-to-moderate AD
  - This analysis includes subgroups of patients with baseline facial and/or eyelid involvement

Outcomes in This Analysis

- vIGA-AD success: clear (0) or almost clear (1) plus ≥2-grade improvement
- EASI-75: ≥75% improvement in EASI (all regions)
- hEASI-75/100: ≥75%/100% improvement in EASI for the head/neck region
- hEASI component scores: change from baseline in erythema, induration/infiltration (papules), excoriation, and lichenification scores in the head/neck region, each rated on a scale of 0 (none) to 3 (severe), with half-point scores (ie, 0.5, 1.5, and 2.5) allowed
- Safety and tolerability

RESULTS

- Of 1337 patients pooled from the INTEGUMENT-1 and -2 trials, 567 (42%) had face and 277 (21%) had eyelid involvement at baseline
- There were significant improvements in signs and symptoms of AD with roflumilast cream 0.15%, compared with vehicle cream
  - Improvements were observed in the overall and baseline face/eyelid involvement groups, as well as for EASI in the head/neck region
  - Achievement of vIGA-AD 0/1 at week 4 in the roflumilast versus vehicle groups, respectively, were
    - Overall: 41.1% vs 21.4%
    - Baseline facial involvement: 36.3% vs 13.7%
    - Baseline eyelid involvement: 37.6% vs 8.9%
- Roflumilast cream 0.15% was well tolerated[7]
  - In the roflumilast group, severe AEs or SAEs were reported for ≤1% of patients, and <2% of patients discontinued the study/study drug because of a TEAE
  - Application-site pain was reported for 1.5% and 0.7% of patients in the roflumilast cream 0.15% and vehicle cream groups, respectively
  - There were minimal cutaneous reactions at the application site, as reported by investigators and patients

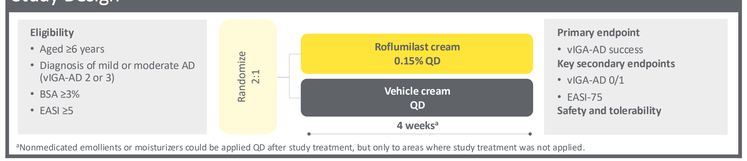
ABBREVIATIONS

AD, atopic dermatitis; AE, adverse event; BSA, body surface area affected; EASI, Eczema Area and Severity Index; hEASI, head/neck-region EASI; ITT, intention to treat; QD, once daily; SAE, serious AE; TCS, topical corticosteroids; TEAE, treatment-emergent AE; vIGA-AD, Validated Investigator Global Assessment of AD; WI-NRS, Worst Itch-Numeric Rating Scale.

REFERENCES

1. AAAAI/ACAAJ JTF Atopic Dermatitis Guideline Panel. *Ann Allergy Asthma Immunol*. 2023;132:274–312. 2. National Eczema Society. Facial eczema. Accessed February 26, 2025. https://eczema.org/information-and-advice/types-of-eczema/facial-eczema/. 3. National Eczema Society. Eczema around the eyes. Accessed February 26, 2025. https://eczema.org/information-and-advice/types-of-eczema/eczema-around-the-eyes/. 4. Silverberg JI, et al. *JAAD*. 2023;89:519–528. 5. Burshtein J, et al. *Dermatol Online J*. 2025;31(1). doi:10.5070/D331164978. 6. Draelos ZD, et al. *J Drugs in Dermatol*. 2024;23:834–840. 7. Simpson EL, et al. *JAMA Dermatol*. 2024;160:1161–1170. 8. ZORVIVE® (roflumilast) cream. Prescribing information. Arcutis Biotherapeutics, Inc.; July 2024. 9. Eichenfield LF, et al. *Pediatric Dermatol*. Published online February 20, 2025. doi:10.1111/pde.15840.

Study Design



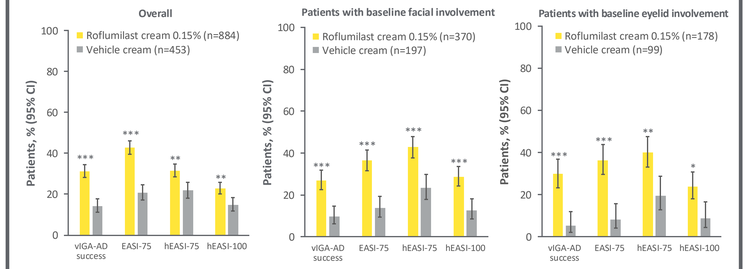
[a]Nonmedicated emollients or moisturizers could be applied QD after study treatment, but only to areas where study treatment was not applied.

Participant Demographics and Baseline Disease Characteristics

		Roflumilast cream 0.15% (n=884)	Vehicle cream (n=453)
Age, mean years, (SD) [range]		27.9 (19.4) [6–91]	27.3 (19.0) [6–84]
Female at birth, n (%)		489 (55.3)	272 (60.0)
Not Hispanic or Latino, n (%)		730 (82.6)	377 (83.2)
Race, n (%)	White	529 (59.8)	267 (58.9)
	Black/African American	176 (19.9)	96 (21.2)
	Asian	114 (12.9)	62 (13.7)
	Other[a]	41 (4.6)	14 (3.1)
	Multiple	24 (2.7)	14 (3.1)
Fitzpatrick skin type, n (%)	I–III	481 (54.4)	238 (52.5)
	IV–VI	403 (45.6)	215 (47.5)
vIGA-AD, n (%)	Mild (2)	211 (23.9)	112 (24.7)
	Moderate (3)	673 (76.1)	341 (75.3)
BSA, %, mean (SD) [range]		13.5 (11.8) [3.0–88.0]	13.9 (11.3) [3.0–86.0]
EASI, mean (SD)		10.1 (5.7)	10.0 (5.2)
Average weekly WI-NRS score, mean (SD)		6.1 (2.2)	5.9 (2.2)
Facial involvement		370 (41.9)	197 (43.5)
Eyelid involvement		178 (20.1)	99 (21.9)

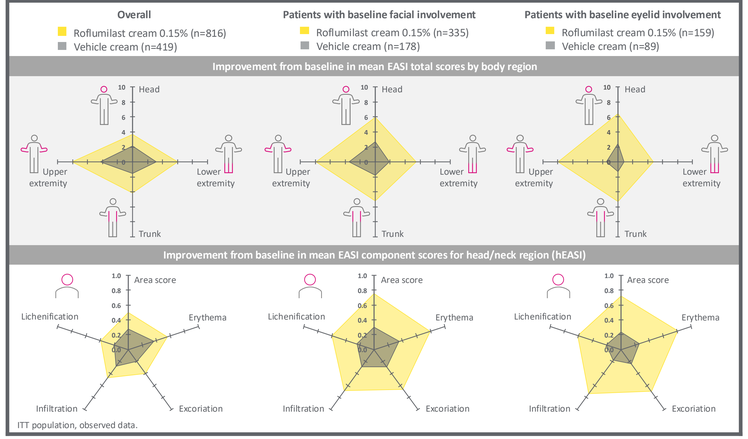
ITT population. [a]Other includes American Indian/Native Alaskan (n=8) and Native Hawaiian/other Pacific Islander (n=1).

Improvement in AD Outcomes at Week 4



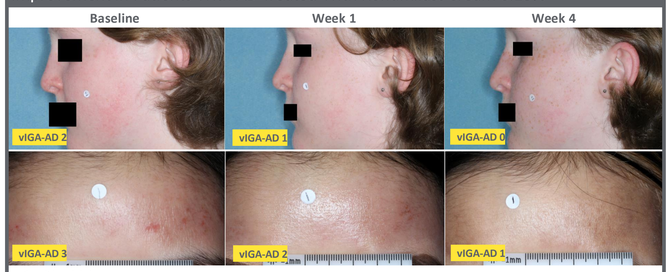
*P<0.01; **P<0.001; ***P<0.0001. ITT population, multiple imputation.

Improvement in Disease Severity From Baseline to Week 4



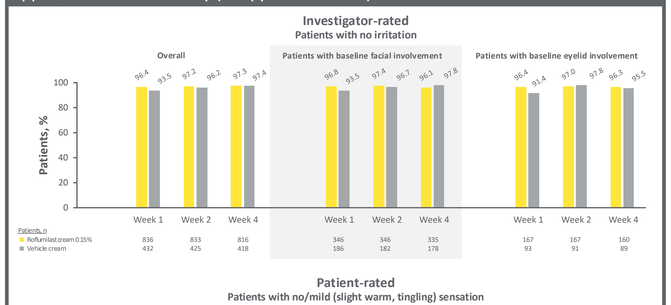
ITT population, observed data.

Improvement in Patients With AD Treated With Roflumilast Cream 0.15%



vIGA-AD is a global measure.

Application-Site Tolerability (all application sites[a])



[a]Outcomes shown for tolerability across all application sites within each patient population. [b]Assessments occurred on day 1 and weeks 1, 2, and 4. Day 1 is the first assessment conducted 10–15 minutes after the first application of study treatment.

CONCLUSIONS

Roflumilast cream 0.15% improved outcomes in patients with AD and disease involvement of the face and/or eyelids.

- After 4 weeks, there were significant improvements in AD with roflumilast, compared with vehicle, across patient groups
- Improvements in severity of EASI components were ≥2-fold higher than vehicle for patients with face/eyelid involvement

Once-daily roflumilast cream 0.15% was well tolerated, with no reactions at the application site.

- Application-site pain was reported for ≤2.2% of patients across treatments and patient groups
- Across all patient groups who received roflumilast
  - Physicians reported no irritation for ≥96% of patients at all time points
  - No/mild sensation was reported by ≥81% of patients after the first application, increasing to ≥92% of patients in weeks 2 and 4

The results of this subpopulation analysis from the phase 3 INTEGUMENT-1 and -2 studies are consistent with previous reports[7,9] and indicate that roflumilast is an appropriate treatment option for those with AD and face and/or eyelid involvement.