Efficacy and Safety of Once-Daily Roflumilast Cream 0.15% for the Treatment of Atopic Dermatitis: Pooled Results in Patients 6 to 17 Years of Age From the INTEGUMENT-1/2 Phase 3 Clinical Trials

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INTRODUCTION

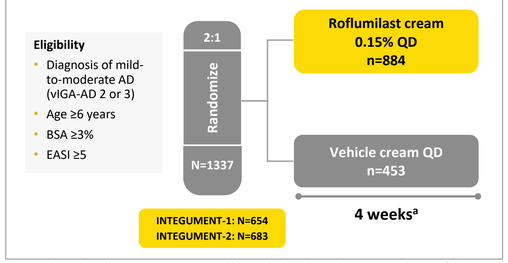
- Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting patients of all age groups
- Roflumilast cream 0.15% is a nonsteroidal drug that has been investigated as a once-daily treatment for patients with AD
  - Does not contain ethanol, propylene glycol, or fragrances that can irritate skin
  - Roflumilast is a phosphodiesterase 4 (PDE4) inhibitor[1,2] with ~25- to >300-fold higher potency than apremilast and crisaborole,[3] with roflumilast more closely mimicking the 3 key binding sites of cyclic adenosine monophosphate to PDE4[4]
- Efficacy and safety of roflumilast cream 0.05% and 0.15% for AD have been demonstrated in Phase 3 randomized trials:
  - Patients aged 2–5 years (INTEGUMENT-PED: NCT04845620)[5]
  - Patient aged ≥6 years (INTEGUMENT-1: NCT04773587; INTEGUMENT-2: NCT04773600)[6,7]
- Here we present pooled efficacy and safety results of roflumilast cream 0.15% in patients aged 6–17 years from the INTEGUMENT-1 and -2 trials

METHODS

- INTEGUMENT-1 and -2 were identical, Phase 3, randomized, double-blind trials
- This subgroup analysis assessed the efficacy and safety of roflumilast cream 0.15% in patients aged 6–11 years and 12–17 years; data are presented alongside data from the overall population

Study Design

Two identical, Phase 3, randomized, double-blind trials



[a]Non-medicated emollients or moisturizers could be applied QD, but only to untreated areas of the patient's skin.
BSA: body surface area; QD: once daily.

Endpoints for This Analysis

- **Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD)**
  - vIGA-AD 0 (Clear)/1 (Almost Clear)
    - Weeks 1, 2, and 4
  - vIGA-AD Success, defined as vIGA-AD 0/1 plus ≥2-grade improvement from baseline
    - Week 4 (primary endpoint)
    - Weeks 1 and 2
- **Eczema Area and Severity Index (EASI)**
  - EASI-75, defined as a ≥75% reduction in EASI score from baseline
    - Weeks 1, 2, and 4
- **Worst Itch-Numeric Rating Scale (WI-NRS)**
  - WI-NRS Success, defined as ≥4-point improvement in patients with baseline WI-NRS score ≥4
    - Weeks 1, 2, and 4

RESULTS

Demographics and Baseline Disease Characteristics

		Roflumilast cream 0.15% (n=884)	Vehicle cream (n=453)
Age, years, mean (SD) [range]		27.9 (19.4) [6–91]	27.3 (19.0) [6–84]
Age group, n (%)	6–11 years	214 (24.2)	103 (22.7)
	12–17 years	192 (21.7)	106 (23.4)
	≥18 years	478 (54.1)	244 (53.9)
Female at birth, n (%)		489 (55.3)	272 (60.0)
Not Hispanic or Latino,[a] n (%)	Not Hispanic or Latino	730 (82.6)	377 (83.2)
Race, n (%)	White	529 (59.8)	267 (58.9)
	Black or African American	176 (19.9)	96 (21.2)
	Asian	114 (12.9)	62 (13.7)
	American Indian or Alaskan Native	7 (0.8)	1 (0.2)
	Native Hawaiian or Other Pacific Islander	1 (0.1)	0
	Other	33 (3.7)	13 (2.9)
	>1 race	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 of 2 (Mild), n (%)	6–11 years	53 (24.8)	29 (28.2)
	12–17 years	48 (25.0)	26 (24.5)
	Overall	211 (23.9)	112 (24.7)
vIGA-AD of 3 (Moderate), n (%)	6–11 years	161 (75.2)	74 (71.8)
	12–17 years	144 (75.0)	80 (75.5)
	Overall	673 (76.1)	341 (75.3)
EASI, mean (median) [range]	6–11 years	11.2 (9.6) [5.0–52.5]	11.0 (8.7) [5.0–37.9]
	12–17 years	10.5 (8.7) [4.4–47.4]	9.7 (8.4) [3.4–25.6]
	Overall	10.1 (8.4) [4.4–52.5]	10.0 (8.4) [3.4–37.9]
BSA, %, mean (median) [range]	6–11 years	17.2 (12.5) [3.0–76.0]	16.8 (13.0) [3.2–86.0]
	12–17 years	14.1 (9.2) [3.0–88.0]	13.8 (9.5) [3.0–52.0]
	Overall	13.5 (9.7) [3.0–88.0]	13.9 (10.0) [3.0–86.0]
Weekly WI-NRS, mean (median) [range]	6–11 years	5.9 (6.1) [0.0-10.0]	5.7 (5.9) [1.0–10.0]
	12–17 years	5.7 (5.9) [0.0–10.0]	5.1 (5.1) [0.0–9.0]
	Overall	6.1 (6.3) [0.0–10.0]	5.9 (6.0) [0.0–10.0]
Facial involvement, n (%)	6–11 years	112 (52.3)	55 (53.4)
	12–17 years	91 (47.4)	44 (41.5)
	Overall	370 (41.9)	197 (43.5)

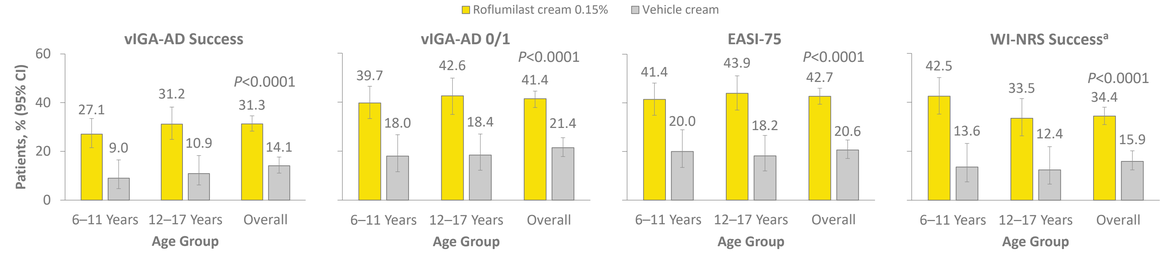
[a]Ethnicity data not reported for 4 patients in each group.

Safety

	6–11 Years		12–17 Years		Overall	
Patients, n (%)	**Roflumilast cream 0.15% (n=214)**	**Vehicle cream (n=103)**	**Roflumilast cream 0.15% (n=192)**	**Vehicle cream (n=105)**	**Roflumilast cream 0.15% (n=885)**	**Vehicle cream (n=451)**
Patients with any TEAE	53 (24.8)	23 (22.3)	44 (22.9)	14 (13.8)	194 (21.9)	65 (14.4)
Patients with any treatment-related TEAE	15 (7.0)	5 (4.8)	12 (6.3)	2 (1.9)	53 (6.0)	12 (2.7)
Patients with any treatment-emergent SAE[a]	2 (0.9)	0	1 (0.5)	0	8 (0.9)	0
Patients with any TEAE leading to discontinuation of trial/trial drug	4 (1.9)	2 (1.9)	1 (0.5)	0	14 (1.6)	5 (1.1)
Most frequently reported TEAEs[b]						
Headache	7 (3.3)	0	8 (4.3)	0	26 (2.9)	4 (0.9)
Nausea	8 (3.7)	0	3 (1.5)	0	17 (1.9)	2 (0.4)
Application-site pain	6 (2.8)	3 (2.9)	1 (0.5)	0	13 (1.5)	3 (0.7)
Diarrhea	3 (1.4)	2 (1.9)	2 (1.1)	0	13 (1.5)	2 (0.4)
Vomiting	8 (3.7)	2 (1.9)	3 (1.6)	0	13 (1.5)	2 (0.4)

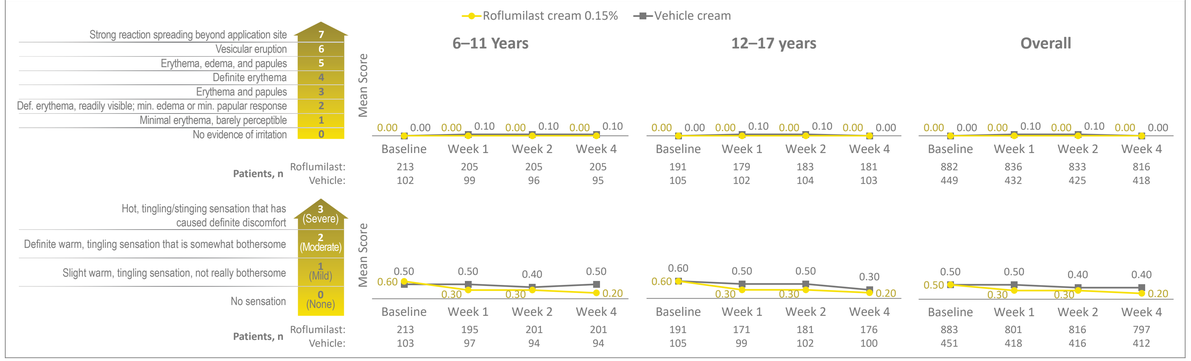
[a]SAEs were atopic dermatitis, cutaneous nerve entrapment, depression, diverticulitis, general physical health deterioration, pulmonary embolism, staphylococcal scalded skin syndrome, suicidal ideation; [b]≥1.5% in the roflumilast group in the overall trial population.
SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Greater Proportions of Patients Treated With Roflumilast Versus Vehicle Achieved vIGA-AD Success, vIGA-AD 0/1, EASI-75, and WI-NRS Success at Week 4, With Similar Results in Age Subgroups Compared With the Overall Population



[a]WI-NRS success assessed in patients with baseline WI-NRS ≥4 only (6–11 years: n=167 [roflumilast] and n=78 [vehicle]; 12–17 years: n=150 and n=74; overall: n=709 and n=349).

Investigator- and Patient-Rated Local Tolerability Was Similar Between Roflumilast Cream and Vehicle Cream Across Age Groups



Def.: definite; min.: minimal.

CONCLUSIONS

- Once-daily, nonsteroidal roflumilast cream 0.15% improved multiple signs and symptoms of AD in pediatric patients aged 6–17 years in 2 Phase 3 trials
  - In the pediatric subgroup, more patients treated with roflumilast achieved vIGA-AD Success, vIGA-AD 0/1, EASI-75, and WI-NRS Success compared with those treated with vehicle, similar to the overall population
- Local tolerability was generally similar between roflumilast and vehicle and rates of TEAEs were low, including application-site pain
  - Local tolerability and rates of TEAEs were generally similar across age groups
- Pediatric subgroups treated with roflumilast experienced similar efficacy and safety to the overall population

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DISCLOSURES

AAH, LFE, ELS, JB, MG, MEG, JJ, VHP, and **LS** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **MSS, DK, PB, DRB, RCH,** and **DHC** are employees of Arcutis Biotherapeutics, Inc.

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