Characterization of Proactive Twice-Weekly Application in Patients With Atopic Dermatitis Treated With Roflumilast Cream 0.15%/0.05%

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Background

Burden of AD

- AD is an inflammatory skin disease that is commonly first diagnosed during childhood; however, it often becomes chronic and persists into adulthood[1,2]
- Historical treatments used to treat AD, such as TCS and TCIs, can have complicated treatment regimens and limitations that impact adherence and efficacy[3,4]

Topical Roflumilast

- Topical treatment options with the potential to be used for proactive, long-term use to maintain disease control are needed, especially in pediatric populations[5,6]
- Topical roflumilast is a potent PDE4 inhibitor–based advanced targeted topical therapy that does not contain ethanol, propylene glycol, formaldehyde-releasing agents, fragrances, or other potentially skin-irritating excipients[7]
- Efficacy, safety, and tolerability of once-daily roflumilast cream 0.05% and 0.15% in patients with AD aged 2–5 years and ≥6 years, respectively, were demonstrated in the 4-week, phase 3 INTEGUMENT-PED (NCT04845620)[8] and INTEGUMENT-1/2 (NCT04662487/NCT04773600)[9] trials

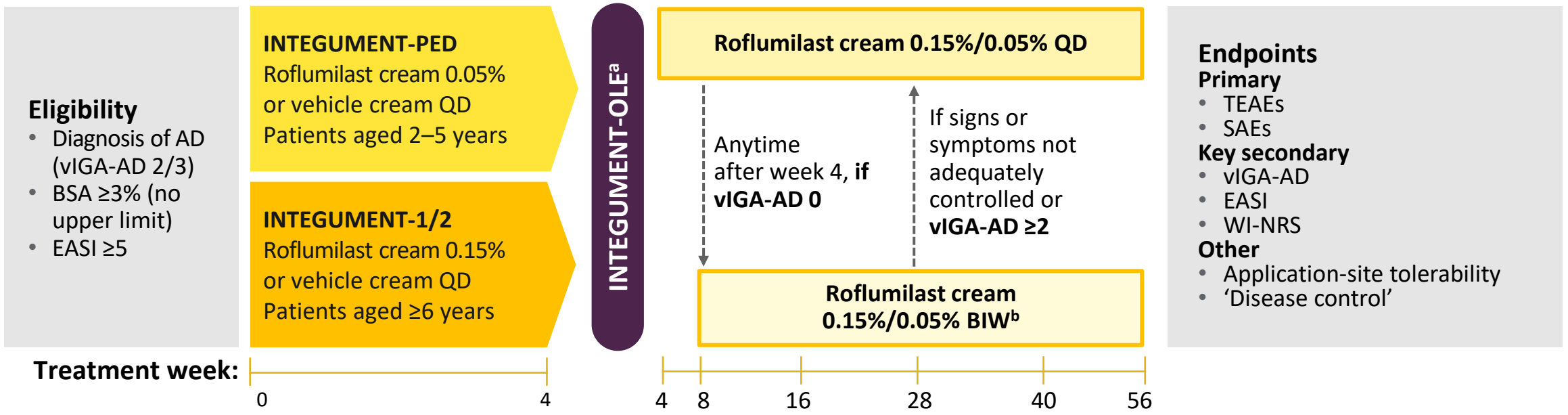
INTEGUMENT-OLE (NCT04804605) investigated the application of roflumilast cream 0.15%/0.05% for up to an additional 52 weeks in patients aged ≥2 years with AD. Control of AD signs and symptoms in patients with clear skin who switched to proactive BIW application[10] is described here.

AD, atopic dermatitis; BIW, twice weekly; PDE4, phosphodiesterase 4; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids.

1. Silverberg JI, et al. *Ann Allergy Asthma Immunol.* 2021;126:417–428. 2. Hadi HA, et al. *Life.* 2021;11:936. 3. Burshtein J, et al. *Dermatol Online J.* 2025;31(1). doi:10.5070/D331164978. 4. Capozza K and Schwartz A. *Pediatr Dermatol.* 2020;37:58–61. 5. Barta K, et al. *Ann Allergy Asthma Immunol.* 2023;130(1):93–99e10. 6. Davis DMR, et al. *J Am Acad Dermatol.* 2025;93(3):745.e1–745.e7. 7. Draelos ZD, et al. *J Drugs Dermatol.* 2024;23:834–840. 8. Eichenfield LF, et al. *Pediatr Dermatol.* 2025;42:296–304. 9. Simpson EL, et al. *JAMA Dermatol.* 2024;160:1161–1170. 10. Wollenberg A, et al. *J Dtsch Dermatol Ges.* 2009;7(2):117–121.

INTEGUMENT-OLE Study Design

INTEGUMENT-OLE was a 52-week, phase 3, multicenter, OLE trial in patients aged ≥2 years with mild-to-moderate AD



Application of nonmedicated emollients or moisturizers was allowed as a part of the patient's stable regimen.

Assessment of disease control

- Disease clearance (ie, vIGA-AD 0) and proportions of patients who switched to BIW application
- Time to initiation of BIW application
- Duration of 'disease control', defined as vIGA-AD 0/1 and adequate control of signs and symptoms with BIW application
- Proportion of patients who maintained BIW application through end of study treatment
- Mean percentage of post–week-4 OLE days patients applied roflumilast BIW

[a]After OLE study enrollment commenced, the protocol was amended to allow patients (aged 2–5 years) who completed INTEGUMENT-PED to enroll, as well as a 24-week cohort consisting of an additional ~550 patients aged 6–17 years. Patients must have successfully completed 4 weeks in a parent trial with no treatment-related AEs or SAEs that precluded further treatment with roflumilast cream. [b]Proactive BIW therapy was maintained as long as signs and symptoms of AD were adequately controlled and vIGA-AD remained clear or almost clear (0/1).

AD, atopic dermatitis; BIW, twice weekly; BSA, body surface area affected; EASI, Eczema Area and Severity Index; QD, once daily; OLE, open-label extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event; vIGA-AD, Validated Investigator Global Assessment for AD; WI-NRS, Worst Itch-Numeric Rating Scale.

Patient Demographics and Baseline Disease Characteristics

		Aged 2–5 years Roflumilast cream 0.05% (n=562)[a]	Aged ≥6 years Roflumilast cream 0.15% (n=658)[b]
Age, mean (median) [range], years		3.3 (3.0) [2–5]	19.7 (13.0) [6–84]
Male sex at birth, n (%)		286 (50.9)	367 (55.8)
Ethnicity, n (%)	Hispanic or Latino	95 (16.9)	109 (16.6)
Race, n (%)	White	399 (71.0)	412 (62.6)
	Black or African American	80 (14.2)	89 (13.5)
	Asian	45 (8.0)	98 (14.9)
	Other/Multiple	38 (6.8)	59 (9.0)
Fitzpatrick skin type, n (%)[c]	Type I–III	374 (66.5)	366 (55.6)
	Type IV–VI	187 (33.3)	292 (44.4)
vIGA-AD, n (%)	Mild (2)	121 (21.5)	172 (26.1)
	Moderate (3)	441 (78.5)	486 (73.9)
Mean (median) [range]	BSA, %	22.3 (17.5) [3.0–82.0]	14.8 (10.5) [3.0–88.0]
	WI-NRS (weekly average)	6.1 (6.0) [0.0–10.0]	5.8 (6.0) [0.0–10.0]
	EASI	12.2 (10.2) [4.6–42.0]	10.5 (8.8) [5.0–52.5]

Safety populations; baseline of parent studies. [a]Patients entering INTEGUMENT-OLE from INTEGUMENT-PED. [b]Patients entering INTEGUMENT-OLE from INTEGUMENT-1/2. [c]There was one missing value in the vehicle group of INTEGUMENT-PED for Fitzpatrick skin type.

BSA, body surface area affected; EASI, Eczema Area and Severity Index; vIGA-AD, Validated Investigator Global Assessment for atopic dermatitis; WI-NRS, Worst Itch-Numeric Rating Scale.

Patients Who Switched to BIW Application

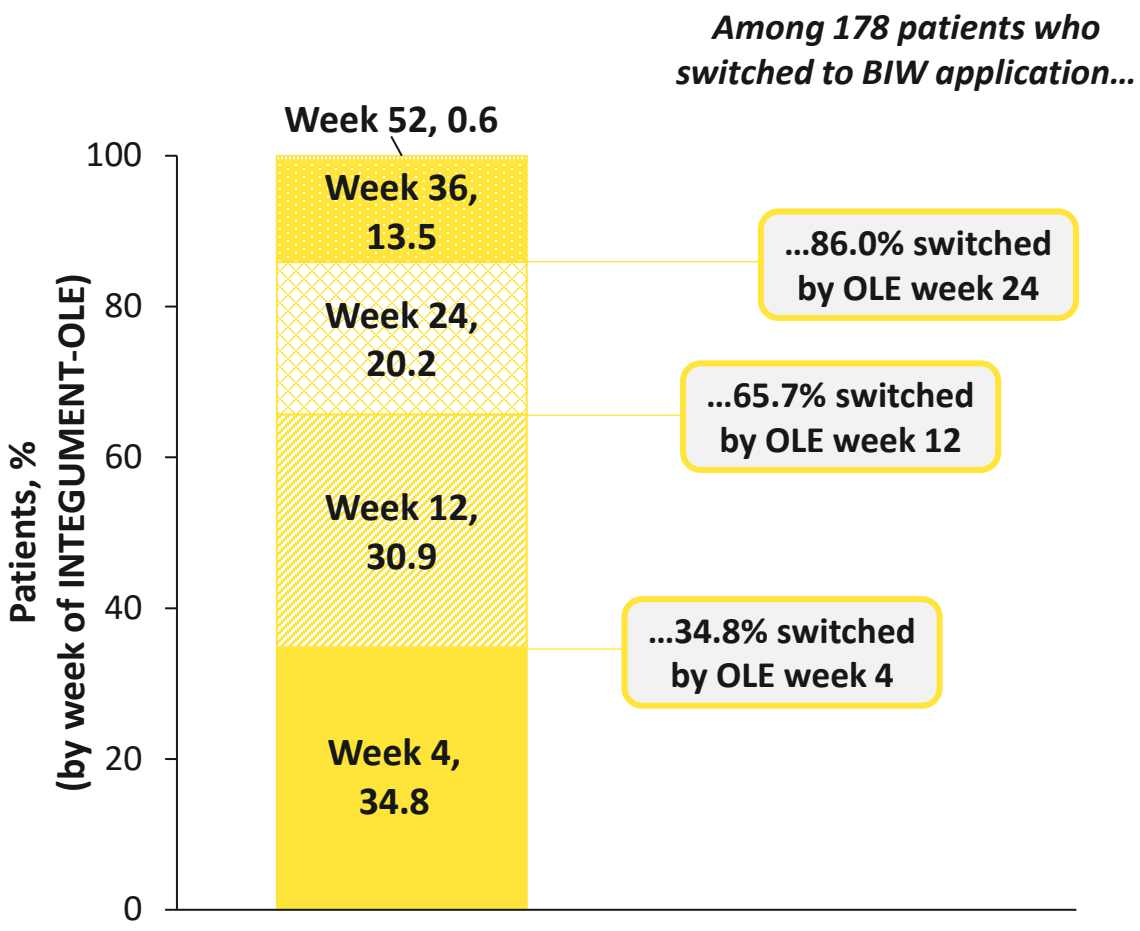
	Switched to proactive BIW application	Maintained BIW dosing through end of treatment	Median duration of 'disease control' with BIW application[a]
Aged 2–5 years Roflumilast cream 0.05%[b]	**31.7% (178/562 patients)**	**54.5% (97/178 patients)**	**238 days** (95% CI, 146–331)
Aged ≥6 years Roflumilast cream 0.15%[c]	**20.1% (132/658 patients)**	**65.2% (86/132 patients)**	**281 days** (95% CI, 147–NE)

[a]Kaplan-Meier median assessed among patients who achieved vIGA-AD 0 and switched to proactive BIW application (n=170 and n=130, respectively). [b]Patients entering INTEGUMENT-OLE from INTEGUMENT-PED. [c]Patients entering INTEGUMENT-OLE from INTEGUMENT-1/2.

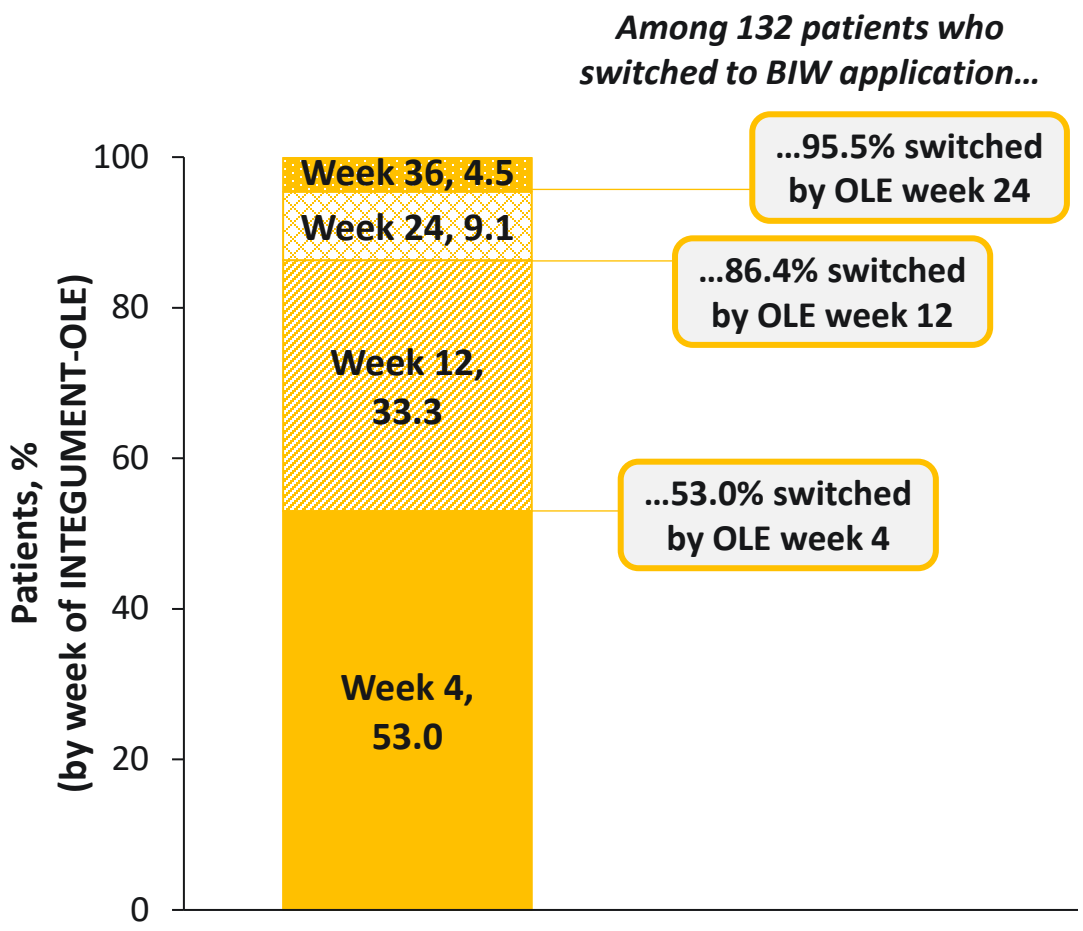
BIW, twice weekly; NE, not evaluable; vIGA-AD, Validated Investigator Global Assessment for atopic dermatitis.

Time to First BIW Application

Aged 2–5 years
Roflumilast cream 0.05%[a]

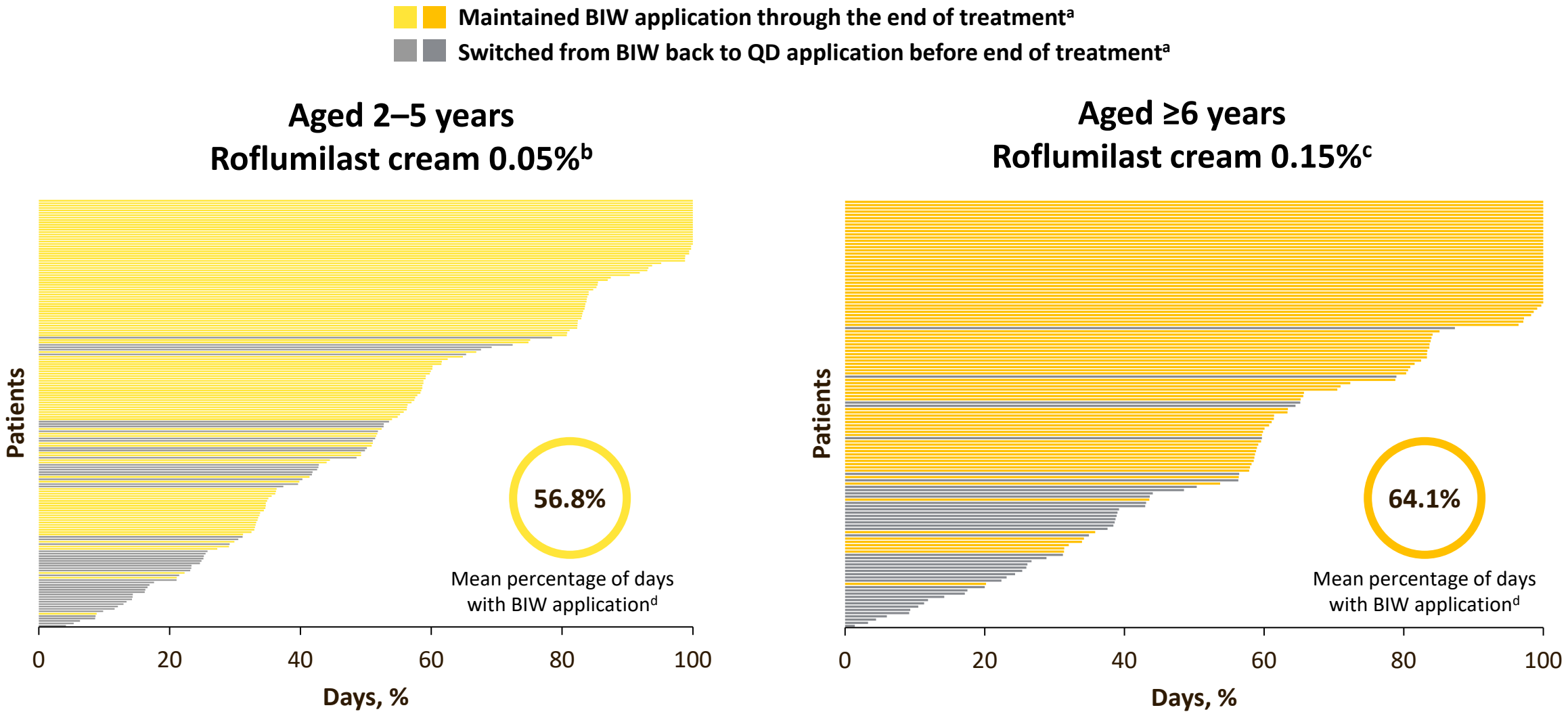


Aged ≥6 years
Roflumilast cream 0.15%[b]



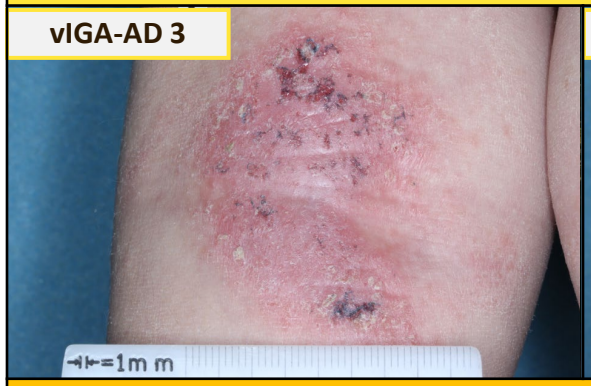
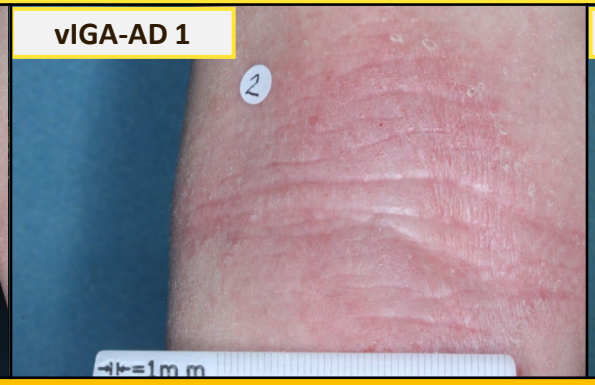
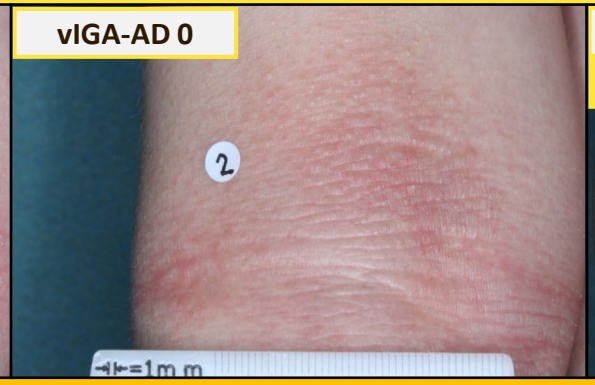
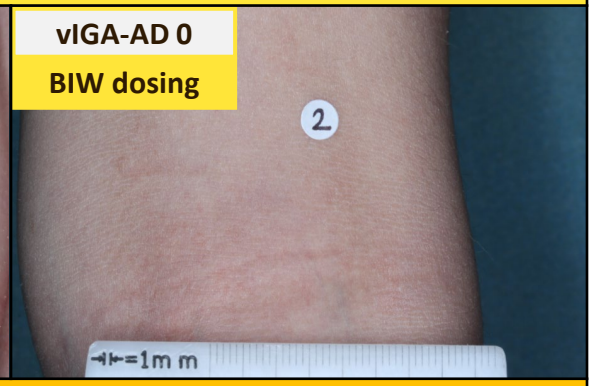
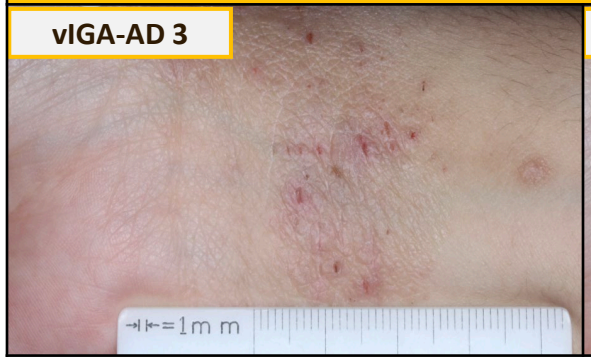
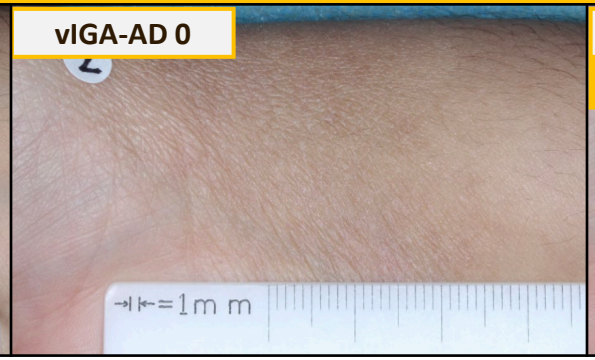
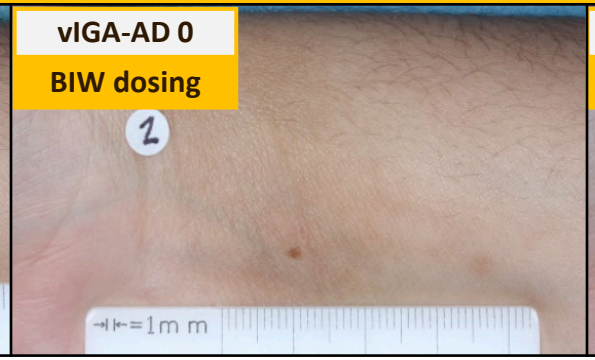
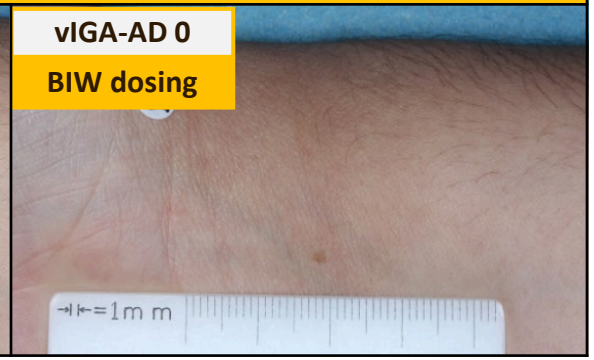
Patients who switched to BIW application of roflumilast cream 0.05%/0.15% at least once during the study. [a]Patients entering INTEGUMENT-OLE from INTEGUMENT-PED. [b]Patients entering INTEGUMENT-OLE from INTEGUMENT-1/2.
BIW, twice weekly.

Time Using Proactive BIW Application for Continuous 'Disease Control'



Patients who switched to BIW application of roflumilast cream 0.05%/0.15% at least once during the study. [a]End of treatment was defined as study completion or discontinuation. [b]Patients entering INTEGUMENT-OLE from INTEGUMENT-PED. [c]Patients entering INTEGUMENT-OLE from INTEGUMENT-1/2. [d]Proportion post-week 4 of INTEGUMENT-OLE.
BIW, twice weekly; QD, once daily.

Improvement in AD With Roflumilast Cream Over Time

Parent study baseline	OLE baseline	OLE week 4	OLE week 52
5-year-old White male with a 5-year history of AD; roflumilast cream 0.05%[a]			
 vIGA-AD 3	 vIGA-AD 1	 vIGA-AD 0	 vIGA-AD 0 BIW dosing
16-year-old White, Hispanic female with a 4-year history of AD and prior inadequate response, intolerance, or contraindication to TCS; roflumilast cream 0.15%[b]			
 vIGA-AD 3	 vIGA-AD 0	 vIGA-AD 0 BIW dosing	 vIGA-AD 0 BIW dosing

Note: The white sticker is placed by investigator for reference. [a]Patients entering INTEGUMENT-OLE from INTEGUMENT-PED. [b]Patients entering INTEGUMENT-OLE from INTEGUMENT-1/2.
AD, atopic dermatitis; BIW, twice weekly; OLE, open-label extension; TCS, topical corticosteroids; vIGA-AD, Validated Investigator Global Assessment for AD.

Conclusions

Among patients who switched to BIW application during the INTEGUMENT-OLE study

- The majority switched by week 12; 54.5% of patients from INTEGUMENT-PED and 65.2% from INTEGUMENT-1/2 maintained the BIW regimen through the end of the study
- The median duration of 'disease control' for patients who switched to BIW application was 238 and 281 days for INTEGUMENT-PED and INTEGUMENT-1/2, respectively
- The mean percentage of days patients were using BIW dosing during the trial was 56.8% and 64.1% for patients from INTEGUMENT-PED and INTEGUMENT-1/2, respectively

Long-term control with reduced dosing frequency is especially impactful among the pediatric population, where adherence is a known issue

Primary safety and efficacy outcomes in patients from the OLE study[1,2] support the use of roflumilast cream 0.15%/0.05% as a long-term treatment option for patients with mild-to-moderate AD, with the potential for proactive therapy with BIW application

AD, atopic dermatitis; BIW, twice weekly; OLE, open-label extension.

1. Simpson EL, et al. *Dermatitis.* 2026;37(1):75–83. doi:10.1089/derm.2024.0418. 2. Eichenfield LF, et al. *Pediatr Dermatol.* Published online March 8, 2026. doi:10.1111/pde.70177.