Roflumilast Cream 0.15% in Patients With Atopic Dermatitis: Individual Patient EASI Responses: Pooled INTEGUMENT-1 and INTEGUMENT-2 Phase 3 Trials

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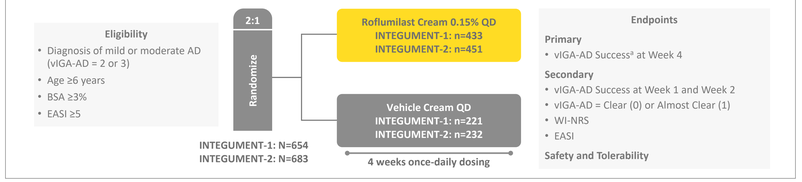
INTRODUCTION

- The Eczema Area and Severity Index (EASI) is used to assess disease severity of atopic dermatitis (AD) in clinical trials[1]
- Topical roflumilast is a once-daily, nonsteroidal treatment, with clinical trials demonstrating the efficacy and safety profile in cream and foam formulations for long-term management of psoriasis, seborrheic dermatitis, and AD[2-4]
- Pooled efficacy and safety results of two Phase 3 clinical trials (INTEGUMENT-1 and INTEGUMENT-2) assessing roflumilast cream 0.15% in patients with AD have been presented previously[5]
- Here we present individual patient EASI responses

METHODS

- INTEGUMENT-1 and INTEGUMENT-2 were identical, Phase 3, randomized, double-blind, vehicle-controlled, 4-week trials of once-daily roflumilast cream 0.15% in patients aged ≥6 years with AD (body surface area [BSA] affected: ≥3%; Figure 1)
- The primary efficacy endpoint was validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success (score of Clear or Almost Clear plus ≥2-grade improvement from baseline) at Week 4
  - EASI scores were evaluated as secondary endpoints

Figure 1. Study Design



[a]vIGA-AD Success = Clear or Almost Clear plus 2-grade improvement from baseline.
AD: atopic dermatitis; BSA: body surface area; EASI: Eczema Area and Severity Index; QD: once daily; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS: Worst Itch-Numeric Rating Scale.

RESULTS

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

Table 1. Patient Baseline Demographics and Disease Characteristics

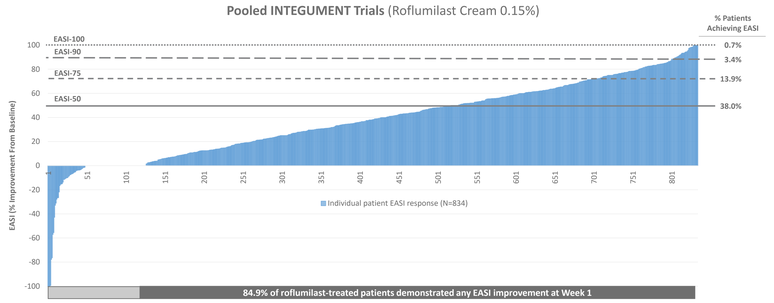
	Roflumilast Cream 0.15% (n=884)	Vehicle (n=453)
Age, years, mean (SD)	27.9 (19.4)	27.3 (19.0)
Sex, n (%)		
Male	395 (44.7)	181 (40.0)
Female	489 (55.3)	272 (60.0)
Baseline vIGA-AD,[a] n (%)		
2 (mild)	211 (23.9)	112 (24.7)
3 (moderate)	673 (76.1)	341 (75.3)
EASI[b]		
Mean (SD)	10.1 (5.7)	10.0 (5.2)
Median (range)	8.4 (4.4–52.5)	8.4 (3.4–37.9)
BSA		
Mean (SD)	13.5 (11.8)	13.9 (11.3)
Median (range)	9.7 (3.0–88.0)	10.0 (3.0–86.0)

[a]A 5-point scale ranging from 0 (Clear) to 4 (Severe) assessing inflammatory signs of AD; [b]A 72-point scale based on AD disease intensity and total affected body area.
AD: atopic dermatitis; BSA: body surface area; EASI: Eczema Area and Severity Index; SD: standard deviation; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis.

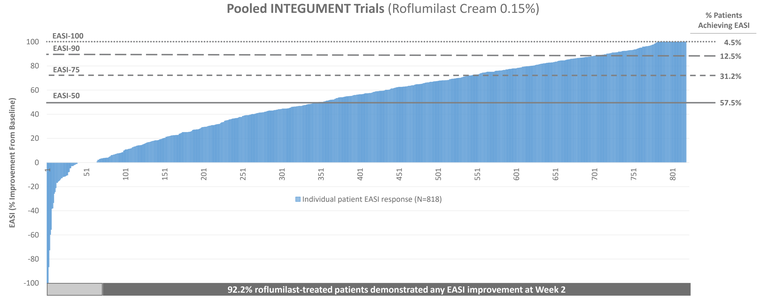
- At Week 4, statistically significantly more roflumilast- than vehicle-treated patients achieved:
  - vIGA-AD Success (31.3% vs 14.1%; *P*<0.0001)[5]
  - vIGA-AD of Clear or Almost Clear (41.1% vs 21.4%; *P*<0.0001)[5]
  - Improvements in itch were observed 24 hours after first application and were greater than vehicle (*P*<0.0001)[5]
- At the first posttreatment time point evaluated (Week 1; Figure 2A), 84.9% of roflumilast-treated patients had a measurable improvement in EASI
  - At Week 4, 92% of roflumilast-treated patients had a measurable improvement in EASI
- Based on observed data (ie, no imputation of missing data), differences favoring roflumilast over vehicle were observed at Week 4 for percentages of patients achieving reduction in EASI:
  - Percentage achieving 50% reduction in EASI: 69.2% vs 44.4% (*P*<0.0001)
  - Percentage achieving 75% reduction in EASI: 44.5% vs 21.2% (*P*<0.0001)
  - Percentage achieving 90% reduction in EASI: 22.4% vs 8.6% (*P*<0.0001)
  - Percentage achieving 100% reduction in EASI: 9.8% vs 4.8% (*P*<0.002)
- Individual EASI responses in roflumilast-treated patients are illustrated in Figures 2A-C

Figure 2. Individual Patient % EASI Improvement From Baseline

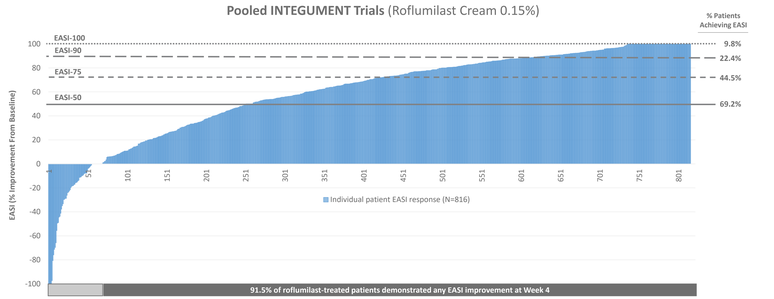
A. Individual Patient % EASI Improvement From Baseline at Week 1



B. Individual Patient % EASI Improvement From Baseline at Week 2



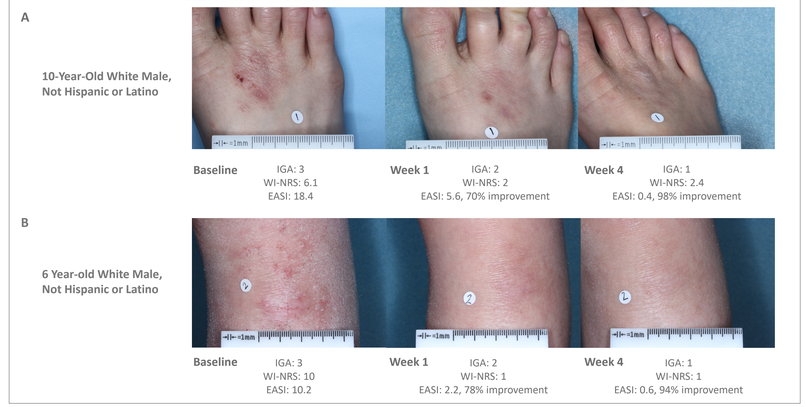
C. Individual Patient % EASI Improvement From Baseline at Week 4



EASI: Eczema Area and Severity Index; EASI-50: 50% reduction in EASI from baseline; EASI-75: 75% reduction in EASI from baseline; EASI-90: 90% reduction in EASI from baseline; EASI-100: 100% reduction in EASI from baseline.

- Patient photographs demonstrating disease improvement over time are shown in Figure 3

Figure 3. Changes in a Patient With AD Treated With Roflumilast Cream 0.15%



AD: atopic dermatitis; EASI: Eczema Area and Severity Index; IGA: Investigator Global Assessment; 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
- On local tolerability assessments, >95% of investigators reported no evidence of irritation at any time point
- >90% of patients reported no or mild sensation after the first application of roflumilast cream 0.15% and subsequent assessment time points on patient-rated local tolerability assessments

CONCLUSIONS

- Roflumilast cream 0.15% provided greater improvement in vIGA-AD Success, vIGA-AD of Clear or Almost Clear, Worst Itch-Numeric Rating Scale, and EASI versus vehicle in patients with AD in two Phase 3 trials
  - Improvements in itch were observed 24 hours after first application and were greater than vehicle
  - 85% of patients treated with roflumilast cream 0.15% demonstrated any improvement in EASI score by Week 1 and 92% of patients by Week 4
- Safety and tolerability were favorable, with nearly all roflumilast- and vehicle-treated patients reporting no or mild sensation at the application site by Week 4

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DISCLOSURES

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