Safety, Efficacy, and Pharmacokinetics of Roflumilast Cream 0.3% Once Daily for Treatment of Plaque Psoriasis in Children Aged 2–11 Years

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INTRODUCTION

- Plaque psoriasis, the most common form of psoriasis, is characterized by erythematous, scaly, and often pruritic plaques
  - The pathogenesis of plaque psoriasis is thought to be generally similar in children and adults[1]
- Limited topical treatments are approved for children <12 years old with psoriasis[2,3]
- Roflumilast cream 0.3%, a potent phosphodiesterase-4 inhibitor, is a once-daily, nonsteroidal treatment approved for psoriasis, including intertriginous areas, in patients ≥12 years old
  - It is formulated as a water-based cream with an emollient emulsifier and without irritating excipients such as propylene glycol, polyethylene glycol, ethanol, or fragrances known to cause irritation and disrupt the skin barrier

METHODS

- Two 4-week, phase 2, open-label, maximal usage pharmacokinetic (PK) and safety studies of roflumilast cream 0.3% were conducted in patients with psoriasis aged 2–5 (Study 216; N=10) years and 6–11 (Study 215; N=20) years
  - At baseline, patients had ≥2% body surface area (BSA) involvement and Investigator Global Assessment (IGA) score of at least Mild (evaluated on a 5-point scale ranging from Clear to Severe; **Table 1**)
  - Caregivers applied roflumilast cream 0.3% to all affected areas once daily for 28 days

Table 1. Baseline Demographics (Safety Population)

	Study 216 (N=10) (2–5 Years of Age)	Study 215 (N=20) (6–11 Years of Age)
Age in years		
Mean (SD)	3.6 (1.26)	8.8 (1.61)
Median (min, max)	4.0 (2, 5)	9.0 (6, 11)
Sex, n (%)		
Male	5 (50.0)	13 (65.0)
Female	5 (50.0)	7 (35.0)
Ethnicity, n (%)		
Hispanic or Latino	9 (90.0)	12 (60.0)
Not Hispanic or Latino	1 (10.0)	8 (40.0)
Race, n (%)		
Black or African-American	9 (90.0)	10 (50.0)
White	1 (10.0)	9 (45.0)
Asian	0	1 (5.0)
BSA affected by psoriasis, %		
Mean (SD)	9.60 (5.275)	8.80 (5.809)
Median (min, max)	9.0 (3.0, 20.0)	8.00 (2.0, 24.0)
BSA <5%	2 (20.0)	6 (30.0)
BSA ≥5%	8 (80.0)	14 (70.0)
IGA, n (%)		
Mild (2)	2 (20.0)	3 (15.0)
Moderate (3)	8 (80.0)	17 (85.0)
Severe (4)	0	0
PASI total score		
Mean (SD)	7.37 (4.134)	8.63 (4.040)
Median (min, max)	7 (2.2, 13.5)	8.00 (2.4, 16.3)
WI-NRS score		
Mean (SD)	7.30 (1.947)	5.00 (2.828)
Median (min, max)	8 (4.0, 10.0)	5.00 (0.0, 9.0)

BSA: body surface area; IGA: Investigator Global Assessment; max: maximum; min: minimum; PASI: Psoriasis Area and Severity Index; SD: standard deviation; WI-NRS: Worst Itch-Numeric Rating Scale.

- The primary endpoints were PK, safety, and tolerability
  - PK samples were collected at Week 4 for all patients and Week 2 for maximal usage subgroups
- Efficacy was evaluated as exploratory endpoints including:
  - IGA Success (IGA of Clear or Almost Clear plus ≥2-grade improvement from baseline)
  - ≥50% improvement and ≥75% improvement on the Psoriasis Area and Severity Index (PASI-50 and PASI-75)
  - Worst Itch-Numeric Rating Scale (WI-NRS) Success (≥4-point reduction in patients with baseline ≥4)
  - Mean change from baseline in BSA
  - Improvement in Children's Dermatology Life Quality Index (CDLQI)

RESULTS

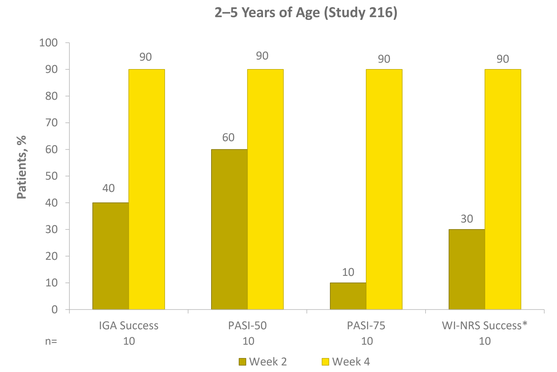
- All patients completed the studies
- At Week 2, mean roflumilast and N-oxide roflumilast pre-dose plasma concentrations were:
  - 2.15 and 22.4 ng/mL, respectively, in those 2–5 years of age (n=9)
  - 3.15 and 28.9 ng/mL, respectively, in those 6–11 years of age (n=10)
- At Week 4, mean roflumilast and N-oxide roflumilast pre-dose concentrations were:
  - 2.04 and 15.8 ng/mL, respectively, in those 2–5 years of age (n=10)
  - 1.68 and 15.7 ng/mL, respectively, in those 6–11 years of age (n=18)
- The percentages of patients aged 2–5 and 6–11 years who achieved IGA Success, PASI-50, PASI-75, and WI-NRS Success at Week 4 are shown in **Figure 1**
- Improvement in CDLQI was observed at Week 4 as compared with that at baseline
  - 9 of the 10 patients aged 2–5 years
  - 13 of the 20 patients aged 6–11 years
- The mean BSA reductions observed in patients aged 2–5 and 6–11 years were 79.1% and 44.4%, respectively
- One patient in the group 2–5 years of age reported a treatment-emergent adverse event (TEAE) of headache, which was considered mild (**Table 2**)
- In the group 6–11 years of age, 4 (20%) patients reported a total of 8 TEAEs; all were considered mild (**Table 2**)
- Favorable local tolerability on investigator- and patient-rated assessments was observed at all measured timepoints (**Tables 3** and **4**)
  - Investigators reported no signs of irritation for 100% of patients in the group 2–5 years of age and ≥85% of patients in the group 6–11 years of age
  - 100% of patients in the group 2–5 years of age and ≥89.5% of patients in the group 6–11 years of age reported no or mild sensation after applying IP

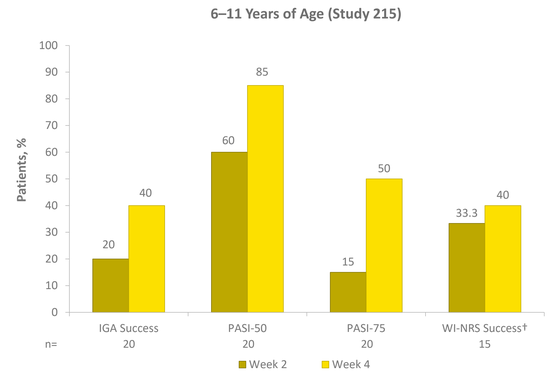
Table 2. Safety

TEAE, n (%)	Study 216 (N=10) (2–5 Years of Age)	Study 215 (N=20) (6–11 Years of Age)
Patients with any TEAE	1 (10.0)	4 (20.0)
Grade 1 TEAE	1 (10.0)	4 (20.0)
Patients with any treatment-related TEAE	0	2 (10.0)
Patients with any SAE	0	0
Patients who discontinued study drug due to AE	0	0
Most common AEs (>2% overall)		
Headache	1 (10.0)	1 (5.0)
Application-site pain	0	1 (5.0)
Back pain	0	1 (5.0)
Candida infection	0	1 (5.0)
Dermatitis	0	1 (5.0)
Nasal congestion	0	1 (5.0)
Perineal erythema	0	1 (5.0)
Perineal pain	0	1 (5.0)

In Study 215, 8 TEAEs were reported in 4 patients; 6 of the TEAEs were reported in 2 patients: 1 patient experienced dermatitis, nasal congestion, perineal pain, and perineal erythema; 1 patient experienced back pain and headache.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Figure 1. Efficacy





*n=10. †n=15.
As observed.
IGA Success: Clear or Almost Clear plus ≥2-grade improvement from baseline; WI-NRS Success: ≥4-point reduction in patients with baseline ≥4; PASI-50: 50% reduction in PASI score; PASI-75: 75% reduction in PASI score.
IGA: Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; WI-NRS: Worst Itch-Numeric Rating Scale.

Table 3. Investigator-Rated Tolerability

Study Visit Category	Study 216 (N=9) (2–5 Years of Age)	Study 215 (N=19) (6–11 Years of Age)
Baseline, n (%)		
0 = No evidence of irritation	9 (100.0)	18 (94.7)
1 = Minimal erythema	0	0
2 = Definite erythema	0	1 (5.3)
Week 2, n (%)	10	20
0 = No evidence of irritation	10 (100.0)	17 (85.0)
1 = Minimal erythema	0	3 (5.0)
Week 4, n (%)	10	20
0 = No evidence of irritation	10 (100.0)	19 (95.0)
1 = Minimal erythema	0	1 (5.0)

Table 4. Patient-Rated Tolerability

Study Visit Category	Study 216 (N=10) (2–5 Years of Age)	Study 215 (N=20) (6–11 Years of Age)
Baseline, n (%)		
0 = None (no sensation)	9 (90.0)	12 (60.0)
1 = Mild (slight warm, tingling sensation; not really bothersome)	1 (10.0)	8 (40.0)
2 = Moderate (definite warm, tingling sensation)	0	0
3 = Severe (hot, tingling/stinging sensation)	0	0
Week 2, n (%)	10	19
0 = None (no sensation)	7 (70.0)	12 (63.2)
1 = Mild (slight warm, tingling sensation; not really bothersome)	3 (30.0)	5 (26.3)
2 = Moderate (definite warm, tingling sensation)	0	2 (10.5)
3 = Severe (hot, tingling/stinging sensation)	0	0

CONCLUSIONS

- Under maximal use conditions in children aged 2–11 years, roflumilast cream 0.3% was well tolerated and improved signs and symptoms of psoriasis with measured improvements in IGA score, PASI score, BSA involvement, CDLQI and WI-NRS
- Overall, PK, safety, tolerability, and efficacy in patients aged 2–11 years were consistent with prior results in adults and adolescents

REFERENCES

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DISCLOSURES

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