Long-term Safety and Efficacy of Roflumilast Cream 0.3% in Adult Patients With Chronic Plaque Psoriasis: Results From a 52-Week, Phase 2b Open-Label Study

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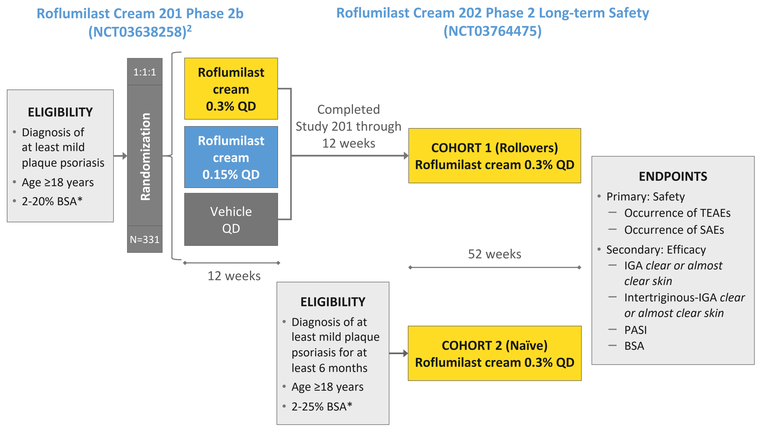
INTRODUCTION

- Current topical treatment options for chronic plaque psoriasis are effective but have limitations including ability to be used chronically, tolerability, and the ability to be used as single agents over the entire body
- Roflumilast cream, a phosphodiesterase-4 (PDE-4) inhibitor that is more potent than other PDE-4 inhibitors,[1] is under investigation as a once-daily, nonsteroidal, topical treatment for psoriasis
- In a phase 2b randomized, double-blind, 12-week trial of 331 adults with chronic plaque psoriasis, roflumilast cream once daily was found to be superior to vehicle cream and was well tolerated[2]
- This multicenter, open-label, 52-week study was also conducted to assess long-term safety of roflumilast 0.3% cream in patients with chronic plaque psoriasis

METHODS

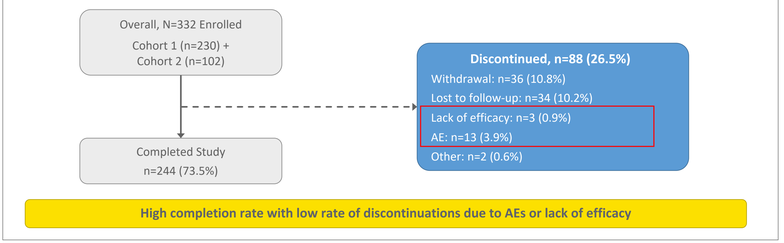
Figure 1. Study Design



*Excludes scalp, palms, soles.
BSA: body surface area; IGA: Investigator Global Assessment; QD: once daily; PASI: Psoriasis Area Severity Index; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

RESULTS

Figure 2. Patient Disposition



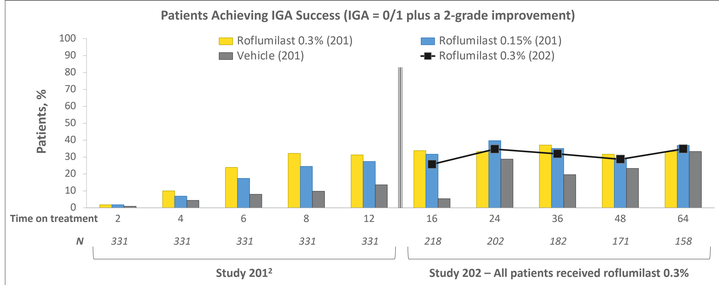
AE: adverse event.

Table 1. Baseline Disease Characteristics

	Cohort 1 Total (n=230)	Cohort 2 Total (n=102)	Overall Total (N=332)
BSA, mean %	6.2	6.6	6.3
PASI, mean	7.2	6.8	7.1
IGA score, n (%)			
1 (almost clear)	8 (3.5)	0 (0.0)	8 (2.4)
2 (mild)	51 (22.2)	17 (16.7)	68 (20.5)
3 (moderate)	156 (67.8)	78 (76.5)	234 (70.5)
4 (severe)	15 (6.5)	7 (6.9)	22 (6.6)
Intertriginous Involvement (I-IGA ≥2)			
I-IGA, n (%)			
2 (mild)	19 (8.3)	12 (11.8)	31 (9.3)
3 (moderate)	17 (7.4)	12 (11.8)	29 (8.7)
4 (severe)	2 (0.9)	0 (0.0)	2 (0.6)

Baseline is defined as the last observation prior to the first dose of roflumilast cream in either the ARQ-151-201 or ARQ-151-202 study.
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous Investigator Global Assessment; PASI: Psoriasis Area and Severity Index.

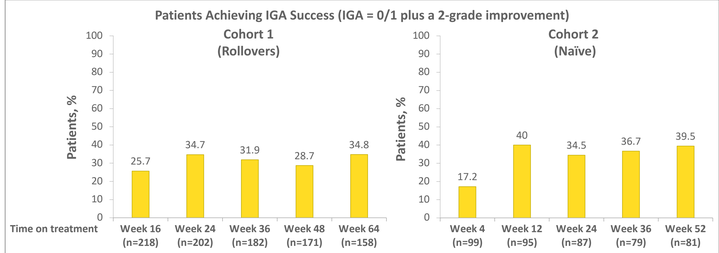
Figure 3. Roflumilast Provided Durable Improvement in IGA



- Among all rollover groups, IGA success was between 33% and 37%, and exceeded that observed among these patients at Week 12 of the parent study

No imputation of missing values. Baseline is defined as the last observation prior to the first dose of ARQ-151 cream in either the ARQ-151-201 or ARQ-151-202 study.
IGA: Investigator Global Assessment.

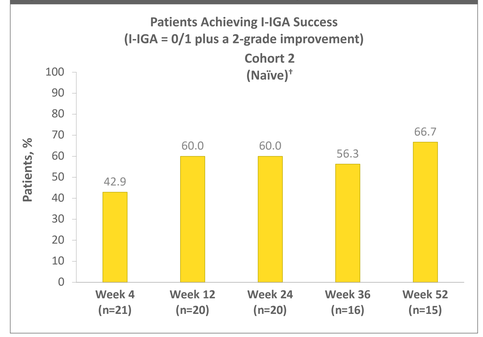
Figure 4. The Proportion of Patients With IGA status of 'Clear' or 'Almost Clear' With Roflumilast Was Consistent Over Time



- Of patients receiving roflumilast cream 0.3% in the parent trial who achieved IGA of clear/almost clear at 12 weeks and continued in the open-label trial, 66.7% achieved IGA of clear/almost clear at 64 weeks or their last visit

IGA: Investigator Global Assessment.

Figure 5. Roflumilast Provided Consistent Improvement of I-IGA‡



†Cohort 1 not shown because I-IGA added as study amendment and numbers of patients evaluated are very small at each timepoint; ‡Collected post-baseline for patients with a severity of at least mild.
I-IGA: Intertriginous-area Investigator Global Assessment.

- 94% of AEs were rated mild or moderate
- 97% of AEs were unrelated or unlikely to be related to treatment as determined by the investigator
- Rates of gastrointestinal and psychiatric AEs were low
- ≥97% of patients had no evidence of irritation per physician assessment at each visit

Table 2. Summary of AEs (Safety Population)

TEAE, n (%)	Cohort 1 Total (n=230)	Cohort 2 Total (n=102)	Overall Total (N=332)
Patients with any TEAE	104 (45.2)	60 (58.8)	164 (49.4)
Patients with any treatment-related TEAE	7 (3.0)	5 (4.9)	12 (3.6)
Patients with any SAE	10 (4.3)	2 (2.0)	12 (3.6)
- Any treatment-related SAE	*0 (0)*	*0 (0)*	*0 (0)*
Patients who discontinued study drug due to AE	11 (4.8)	2 (2.0)	13 (3.9)

TEAE defined as event with an onset on or after the date of the first study drug application in ARQ-151-202 study.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Table 3. Most Common AEs (>2% Overall)

TEAE, n (%)	Cohort 1Total (n=230)	Cohort 2 Total (n=102)	Overall Total (N=332)
Upper respiratory tract infection/viral URTI	14 (6.1)	8 (7.8)	22 (6.6)
Urinary tract infection	9 (3.9)	4 (3.9)	13 (3.9)
Nasopharyngitis	8 (3.5)	5 (4.9)	13 (3.9)
Sinusitis/chronic sinusitis	3 (1.3)	6 (5.9)	9 (2.7)
Hypertension/ essential hypertension	8 (3.5)	1 (1.0)	9 (2.7)
Arthralgia	7 (3.0)	1 (1.0)	8 (2.4)
Back pain	5 (2.2)	2 (2.0)	7 (2.1)
Cough	4 (1.7)	3 (2.9)	7 (2.1)

AE: adverse event; TEAE: treatment-emergent adverse event; URTI: upper respiratory tract infection.

CONCLUSIONS

- Patients with chronic plaque psoriasis need topical treatments that provide effective control of psoriasis with low incidence of side effects that can be used for long-term treatment
- In this phase 2 long-term safety study, roflumilast cream, an investigational, once-daily, nonsteroidal topical PDE-4 inhibitor, was well-tolerated with no new safety signals
  - Rates of discontinuations due to AEs and lack of efficacy were low
- Durable efficacy was observed and the effect was maintained through 52 weeks of treatment in this long-term safety study and up to 64 weeks including the phase 2b study
  - Similar durability of effect was observed in patients with intertriginous area involvement
- Once-daily roflumilast cream is a promising therapy for treating plaque psoriasis

REFERENCES

1. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413-422.
2. Lebwohl MG, et al. *N Engl J Med* 2020;383:229-239.

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