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Rocatinlimab With Concomitant Topical Therapy Significantly Improved Clinical Signs and Symptoms of Atopic Dermatitis in Adults: Results From the Phase 3 ROCKET-SHUTTLE Trial

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Introduction

OX40 receptor (OX40R) plays a key role in atopic dermatitis (AD), driving T-cell imbalance and amplifying proinflammatory activity of OX40R+ pathogenic T cells. Rocatinlimab (ROCA; AMG 451/KHK4083) is a T-cell-rebalancing therapy that inhibits and reduces pathogenic T cells by targeting OX40R. The global ROCKET program is evaluating ROCA in adults and adolescents with moderate-to-severe AD.[1] In ROCKET-HORIZON (NCT05651711)[2] and IGNITE (NCT05398445)[3], ROCA Q4W monotherapy significantly improved AD signs and symptoms in adults vs placebo (PBO). From ROCKET- SHUTTLE (NCT05724199), we report results of ROCA with topical corticosteroids and/or topical calcineurin inhibitors (TCS/TCI).

Materials and Methods

746 adults ≥18 years with AD and an inadequate response to TCS (medium-to-high potency)/TCI were randomized (5:4:4) to ROCA 300 mg, ROCA 150 mg or PBO Q4W (plus Wk-2 loading dose) for 24 wks. Concomitant TCS (low-to-medium potency)/TCI were initiated on study Day 1 and tapered based on clinical response. Coprimary endpoints (Wk 24) were ≥75% reduction from baseline in EASI (EASI 75) and a vIGA-AD™ 0 (clear) or 1 (almost clear) with a ≥2-point reduction from baseline. Key secondary endpoints included a ≥90% reduction from baseline in EASI (EASI 90) at Wk 24, EASI 75 and vIGA-AD 0/1 at Wk 16, and a ≥4-point reduction in the weekly average of the daily worst pruritus numeric rating scale at Wk 24. Rescue therapy (RT; high- to super-high–potency TCS or systemics) was permitted from Day 1. Efficacy analyses included all randomized patients, with RT users considered nonresponders and missing data imputed using nonresponder imputation. Safety analyses included all patients receiving ≥1 dose of study drug.

Results

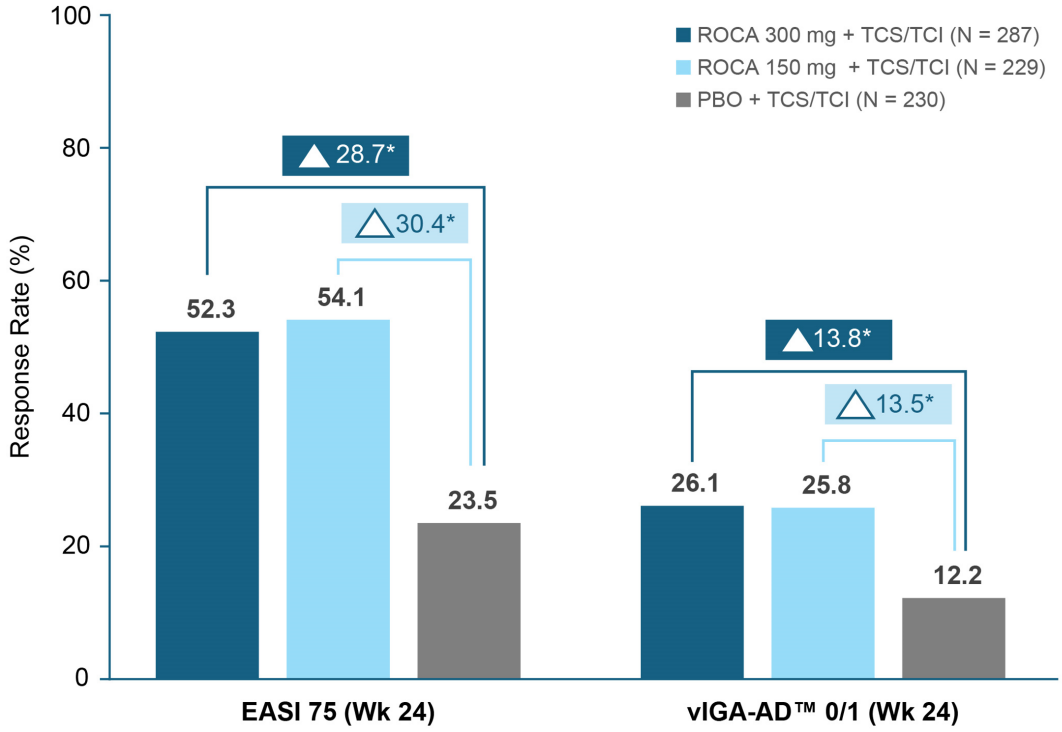
Demographics were well balanced across a diverse global population (Table 1); 59.1% of patients had prior systemic therapy for AD, and 25.3% had prior biologics or systemic JAK inhibitors. Both ROCA arms met the coprimary endpoints (Fig 1; EASI 75 Wk 24, 52.3% [ROCA 300 mg] and 54.1% [ROCA 150 mg] vs 23.5% [PBO]; vIGA-AD 0/1 Wk 24, 26.1% and 25.8% vs 12.2%; all comparisons $P<0.001$) and all key secondary endpoints (data not shown). Progressive efficacy was observed, with no apparent plateau at Wk 24 for the coprimary endpoints (data not shown). TEAEs were balanced across treatment arms (patient incidence of any TEAE, 71.5% [both ROCA arms] vs 67.2% [PBO]; infections, 35.4% [ROCA 300 mg] and 39.9% [ROCA 150 mg] vs 38.0% [PBO]). Incidence of SAEs was higher for ROCA vs PBO (ROCA 300 mg, 3.1%; ROCA 150 mg, 4.4%; PBO, 0.9%); no SAE preferred term was reported by ≥1 patient, and few patients discontinued study drug due to SAEs (ROCA 300 mg, 3/288 [1.0%]; ROCA 150 mg, 4/228 [1.8%]; PBO, 1/229 [0.4%]).

Table 1. ROCKET-SHUTTLE Study Population Demographics and Disease Characteristics

	ROCA 300 mg +TCS/TCI (N=287)	ROCA 150 mg +TCS/TCI (N=229)	PBO +TCS/TCI (N=230)	Total (N=746)
Age, years, mean ± SD	38.8 ± 14.8	38.2 ± 14.3	37.5 ± 14.7	38.2 ± 14.6
Female, n (%)	107 (37.3)	101 (44.1)	95 (41.3)	303 (40.6)
Hispanic/Latino, n (%)	23 (8.0)	17 (7.4)	17 (7.4)	57 (7.6)
Race, n (%)				
White	170 (59.2)	137 (59.8)	132 (57.4)	439 (58.8)
Asian	88 (30.7)	69 (30.1)	78 (33.9)	235 (31.5)
Black or African American	20 (7.0)	16 (7.0)	12 (5.2)	48 (6.4)
Other*	9 (3.1)	7 (3.1)	8 (3.5)	24 (3.2)
Region, n (%)				
Europe	106 (36.9)	90 (39.3)	81 (35.2)	277 (37.1)
North America	97 (33.8)	69 (30.1)	77 (33.5)	243 (32.6)
Asia	68 (23.7)	53 (23.1)	56 (24.3)	177 (23.7)
Other†	16 (5.5)	17 (7.4)	16 (6.9)	49 (6.6)
vIGA-AD™ score,‡ n (%)				
Moderate (score=3)	175 (61.0)	138 (60.3)	137 (59.6)	450 (60.3)
Severe (score=4)	112 (39.0)	91 (39.7)	93 (40.4)	296 (39.7)
EASI total score (0–72),‡ mean ± SD	29.5 ± 11.7	29.1± 10.0	28.9 ±11.2	29.2 ±11.0
Moderate (score ≤21), n (%)	88 (30.6)	54 (23.6)	69 (30.0)	211 (28.3)
Severy/very severe (score >21), n (%)	199 (69.4)	175 (76.4)	161 (70.0)	535 (71.7)
BSA of AD involvement (0%–100%),‡ mean ± SD	45.41 ± 22.57	44.92 ± 21.14	43.60 ± 22.00	44.70 ± 21.95
Prior systemic use, n (%)	164 (57.1)	136 (59.4)	141 (61.3)	441 (59.1)
Prior biologics or systemic JAK inhibitor use, n (%)	66 (23.0)	58 (25.3)	65 (28.3)	189 (25.3)

*Race category of “Other” included American Indian or Alaska native, native Hawaiian or other Pacific Islander, and multiple races. †Region category of “Other” included Australia and Argentina. ‡Baseline vIGA-AD score, EASI score, and BSA were assessed after the first dose of study drug on Day 1.
AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; JAK, Janus kinase; PBO, placebo; ROCA, rocatinlimab; SD, standard deviation; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids; vIGA-AD™, validated Investigator Global Assessment for AD.

Figure 1. Significantly higher proportion of patients receiving ROCA vs PBO in combination with TCS/TCI achieved the coprimary endpoints of EASI-75 and vIGA-AD 0/1 at Wk 24



▲ is the risk difference vs PBO; *$P < 0.001$.
EASI 75, a ≥ 75% improvement from baseline Eczema Area and Severity Index (EASI) score; PBO, placebo; ROCA, rocatinlimab; TCS/TCI, topical corticosteroids and/or topical calcineurin inhibitors; vIGA-AD™, validated Investigator Global Assessment for Atopic Dermatitis; vIGA-AD 0/1, vIGA-AD 0 (clear) or 1 (almost clear) at W24 with ≥ 2-point reduction from baseline; Wk, Week.

Conclusion

In a diverse, treatment-experienced AD patient population failing prior topicals, ROCA with concomitant TCS (low-to-medium potency)/TCI demonstrated statistically significant and clinically meaningful improvements vs PBO in AD clinical signs and symptoms with progressive efficacy and no plateau at Wk 24. ROCA combination therapy was well tolerated, and TEAEs were consistent with adult monotherapy studies. With the ROCKET-HORIZON and IGNITE monotherapy studies, ROCKET-SHUTTLE supports the efficacy and safety of ROCA administered with TCS/TCI.

References:

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