Efficacy and Safety of Crisaborole in Patients ≥3 Months of Age With Mild-to-Moderate Atopic Dermatitis (AD)

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CrisADe

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INTRODUCTION

- Crisaborole ointment, 2%, is an anti-inflammatory nonsteroidal PDE4 inhibitor that is currently approved for the treatment of mild-to-moderate AD in patients aged ≥2 years[1]
- FDA approval was based on efficacy and safety demonstrated in 2 identically designed, randomized, double-blind, vehicle-controlled phase 3 studies (CrisADe CORE 1 [AD-301] and CrisADe CORE 2 [AD-302]) that included patients aged ≥2 years[1]
- CrisADe CARE 1 was a multicenter, open-label, single-arm, phase 4 study designed to evaluate the safety of crisaborole in infants aged 3 months to <2 years with mild-to-moderate AD

OBJECTIVE

- **To examine the efficacy and safety of crisaborole across age groups in the phase 3 studies CORE 1 and CORE 2, and in the phase 4 study, CARE 1**

METHODS

Patients

- Patients aged 3 months to <2 years (CARE 1, NCT03356977) or ≥2 years (CORE 1, NCT02118766; CORE 2, NCT02118792) with mild-to-moderate AD received twice-daily crisaborole (or vehicle in CORE 1/CORE 2) for 28 days

Endpoints

- In CORE 1/CORE 2, the primary endpoint was ISGA success (clear [0] or almost clear [1] with a ≥2-grade improvement from baseline) at day 29; ISGA clear or almost clear at day 29 and safety were secondary endpoints
- In CARE 1, safety was the primary endpoint and ISGA success and ISGA clear or almost clear at day 29 were exploratory endpoints

RESULTS

Patients

- In CORE 1/CORE 2 and CARE 1 combined, 1153 patients with mild-to-moderate AD were treated with crisaborole and included in this analysis, including 137 infants (3 months to <2 years) in CARE 1 and 1016 children, adolescents, and adults in CORE 1/CORE 2 (**Table 1**); 506 patients treated with vehicle in CORE 1/CORE 2 were not included in this analysis
  - Within each age group the majority of patients had moderate AD per ISGA

Table 1. Demographics and Baseline Disease Characteristics Among Crisaborole-Treated Patients (Intent-to-Treat Population)

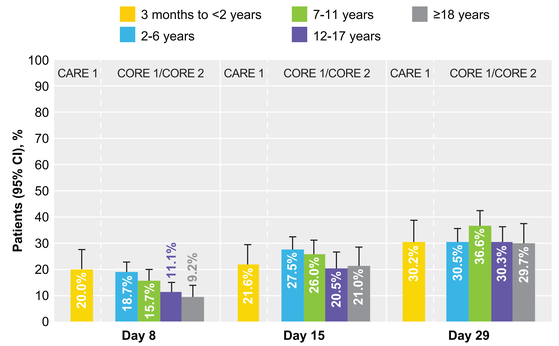
	CARE 1	CORE 1/CORE 2			
	3 months to <2 years N=137	2-6 years N=335	7-11 years N=292	12-17 years N=247	≥18 years N=142
Male, n (%)	88 (64.2)	170 (50.8)	129 (44.2)	109 (44.1)	42 (29.6)
White, n (%)	84 (61.3)	211 (63.0)	173 (59.3)	152 (61.5)	81 (57.0)
ISGA, n (%)					
Mild (2)	52 (38.0)	125 (37.3)	116 (39.7)	92 (37.3)	60 (42.3)
Moderate (3)	84 (61.3)	210 (62.7)	176 (60.3)	155 (62.8)	82 (57.8)
%BSA					
Mean (SD)	28.1 (22.0)	20.1 (19.1)	18.8 (18.6)	17.5 (17.7)	14.6 (13.8)
Median (range)	19.0 (5-94)	12.0 (5-95)	12.0 (5-95)	10.0 (5-90)	9.5 (5-70)
Duration since onset, months/years[a]					
Mean (SD)	10.2 (6.3)	3.3 (1.6)	6.9 (2.9)	10.6 (4.9)	21.6 (16.2)
Median (range)	8.6 (0.0-23.8)	3.1 (0.0-7.0)	7.4 (0.0-11.7)	12.4 (0.0-17.6)	18.5 (0.0-75.2)
Prior medication, n (%)					
TCS	72 (52.6)	161 (48.1)	116 (39.7)	86 (34.8)	44 (31.0)
TCI	2 (1.5)	10 (3.0)	5 (1.7)	11 (4.5)	7 (4.9)

[a]Months for CARE 1, years for CORE 1/CORE 2.

Efficacy

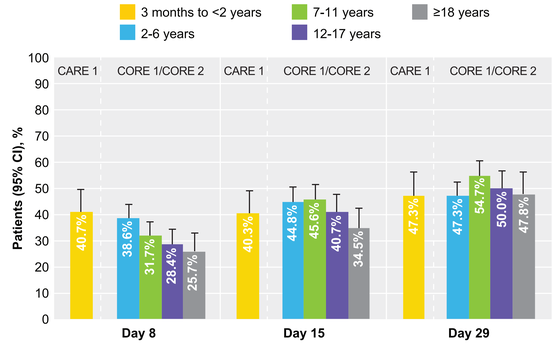
- In CARE 1, 30.2% of infants achieved ISGA success at day 29, consistent with ISGA success rates observed across age groups for crisaborole-treated patients in CORE 1/CORE 2 (**Figure 1**)
- After 1 week of treatment (day 8) with crisaborole, up to 40% of patients achieved ISGA clear or almost clear, and response rates improved across all age groups at day 29 (**Figure 2**)

Figure 1. Proportion of Crisaborole-Treated Patients With ISGA Success



ISGA success defined as clear (0) or almost clear (1) with ≥2-grade improvement.

Figure 2. Proportion of Crisaborole-Treated Patients With ISGA Clear or Almost Clear



Safety

- The majority (≥93%) of TEAEs across all age groups were mild or moderate in severity
- Application site pain was the most common treatment-related AE in all patient age groups (**Table 2**)
  - Rates of treatment-related application site pain/discomfort reported in infants in CARE 1 were consistent with the rate of application site pain reported for crisaborole-treated patients in CORE 1/CORE 2 across age groups

Table 2. Adverse Event Summary for Crisaborole-Treated Patients (Safety Population)

	CARE 1	CORE 1/CORE 2			
	3 months to <2 years N=137	2-6 years N=333	7-11 years N=292	12-17 years N=246	≥18 years N=141
Any TEAE, n (%)	88 (64.2)	115 (34.5)	79 (27.1)	64 (26.0)	38 (27.0)
Serious TEAEs, n (%)	1 (0.7)	2 (0.6)	3 (1.0)	2 (0.8)	0
TEAEs leading to study drug discontinuation, n (%)	4 (2.9)	6 (1.8)	5 (1.7)	2 (0.8)	0
Any treatment-related AEs, n (%)	22 (16.1)	24 (7.2)	23 (7.9)	16 (6.5)	11 (7.8)
Treatment-related AEs in ≥3 patients in any age group, n (%)					
Application site pain	5 (3.6)	12 (3.6)	16 (5.5)	10 (4.1)	7 (5.0)
Application site discomfort	4 (2.9)	0	0	0	0
Application site erythema	3 (2.2)	1 (0.3)	2 (0.7)	1 (0.4)	0
Erythema	4 (2.9)	1 (0.3)	0	1 (0.4)	0
Pruritus	3 (2.2)	1 (0.3)	0	0	0

CONCLUSIONS

- **Based on these studies, crisaborole was effective and well tolerated in patients ≥3 months of age with mild-to-moderate AD**
  - **Rates of reported all-cause TEAEs were generally numerically greater for patients aged 3 months to <2 years than for those aged ≥2 years; however, rates of reported treatment-related application site pain were consistent across age groups (<6%)**
  - **Improvements in AD were observed after 1 week of crisaborole treatment (day 8) and continued to improve through day 29**
- **Efficacy and safety of crisaborole in infants from the CARE 1 study were consistent with those observed in patients aged ≥2 years from the phase 3 studies**

Abbreviations **%BSA**, percentage of treatable body surface area; **AD**, atopic dermatitis; **AE**, adverse event; **FDA**, US Food and Drug Administration; **ISGA**, Investigator's Static Global Assessment; **PDE4**, phosphodiesterase 4; **SD**, standard deviation; **TCS**, topical corticosteroid; **TCI**, topical calcineurin inhibitor; **TEAE**, treatment-emergent adverse event.

References **1.** Paller AS et al. *J Am Acad Dermatol*. 2016;75:494-503.e496.

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