Efficacy and Safety of Crisaborole in Patients With Mild-to-Moderate Atopic Dermatitis With and Without Comorbid Allergic Rhinitis

Jonathan M. Spergel,[1] Michael S. Blaiss,[2] Peter Lio,[3,4] Aharon Kessel,[5,6] Liza Takiya,[7] John L. Werth,[7] Michael A. O'Connell,[7] Chuanbo Zang,[7] Michael J. Cork[8]

[1]Children's Hospital of Philadelphia and Perelman School of Medicine at University of Pennsylvania, Philadelphia, PA, USA; [2]Medical College of Georgia at Augusta University, Augusta, GA, USA; [3]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [4]Chicago Integrative Eczema Center, Chicago, IL, USA; [5]Bnai Zion Medical Center, Haifa, Israel; [6]Bruce and Ruth Rappaport Faculty of Medicine, Technion, Haifa, Israel; [7]Pfizer Inc., Collegeville, PA, USA; [8]Sheffield Dermatology Research, IICD, University of Sheffield, Sheffield Children's Hospital, Sheffield, United Kingdom

Acknowledgments

Editorial/medical writing support under the guidance of the authors was provided by Christopher M. Goodwin, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med.* 2015;163:461-464).

~~Presented at Maui Derm for Dermatologists 2021; January 25-29, 2021~~

INTRODUCTION

- AD is a chronic inflammatory skin disease; patients with AD are at higher risk for other atopic comorbidities, such as allergic rhinitis[1]
  - Based on 1 study in the United States, the 1-year prevalence of allergic rhinitis among adults is 28%[2]
  - Although it is not clear whether the presence of atopic comorbidities makes AD more difficult to treat, there is an association between the presence of atopic conditions such as allergic rhinitis and more severe AD, and there is the possibility that some atopic comorbidities can lead to worsening of underlying AD[3]
- Crisaborole ointment, 2%, is an anti-inflammatory nonsteroidal PDE4 inhibitor for the treatment of patients aged ≥3 months (≥2 years outside the United States)[4] with mild-to-moderate AD
  - Initial regulatory approval was based on the results from 2 identically designed, vehicle-controlled, phase 3 clinical studies: CORE 1 (NCT02118766) and CORE 2 (NCT02118792)[5]

OBJECTIVE

- **To ascertain the efficacy and safety of crisaborole for the treatment of AD in patients with or without allergic rhinitis in a post hoc pooled analysis from the phase 3 studies CORE 1 and CORE 2**

METHODS

Patients and Treatment

- CORE 1 and CORE 2 were identically designed, randomized, double-blind, vehicle-controlled, phase 3, studies to compare crisaborole with vehicle in patients with AD per Hanifin and Rajka criteria[6] who had mild-to-moderate disease per the ISGA and had %BSA of ≥5 (excluding the scalp)
- Patients were randomly assigned in a 2:1 ratio to receive crisaborole ointment, 2%, or vehicle applied twice daily to all areas affected by AD, except the scalp, for 28 days
- For this post hoc analysis, patients were stratified based on their past medical history of allergic rhinitis

Outcomes and Assessments

- The ISGA, which is a 5-point, physician-reported scale of AD severity,[5] was assessed at baseline and weekly thereafter
- Pruritus severity was assessed using the SPS, a validated, patient-/caregiver-reported, 4-point rating scale,[7] and reported twice daily (morning and evening) via electronic diary
- Efficacy outcomes were
  - Proportion of patients who achieved ISGA success (defined as an ISGA of clear [0] or almost clear [1] with a ≥2-grade improvement from baseline) at day 29
  - Proportion who achieved ISGA clear (0) or almost clear (1) at day 29
  - Proportion who showed improvement in SPS score (defined as a weekly average SPS score ≤1 point with ≥1-point improvement from baseline) at week 4
- Safety outcomes were TEAEs (both all cause and treatment related), serious AEs, and AEs of special interest (ie, allergic rhinitis exacerbation)

RESULTS

Patients

- In the pooled study population, 1016 patients received crisaborole and 506 received vehicle
  - Among them, 242 were reported to have a past medical history of allergic rhinitis and 1280 did not have a past medical history of allergic rhinitis
  - Baseline demographics and disease characteristics were generally balanced between treatment arms and between patients who did and those who did not have allergic rhinitis; however, for patients with a past medical history of allergic rhinitis, a relatively greater proportion used systemic corticosteroids, used antihistamines concurrently, and had greater mean %BSA involvement with AD lesions (**Table 1**)

Table 1. Baseline Demographics and Disease Characteristics in Patients With and Patients Without Allergic Rhinitis

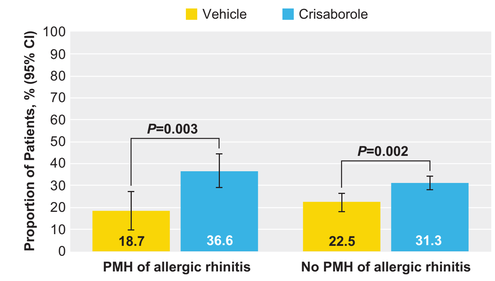
Demographic or Characteristic	PMH of Allergic Rhinitis		No PMH of Allergic Rhinitis	
	Vehicle n=79	Crisaborole n=163	Vehicle n=427	Crisaborole n=853
Age, y				
Mean (SD)	10.9 (8.5)	11.7 (9.4)	12.3 (12.1)	12.4 (12.6)
Median (min, max)	9.0 (2, 45)	10.0 (2, 59)	9.0 (2, 79)	9.0 (2, 79)
Female, % (n)	68.4 (54)	48.5 (79)	53.2 (227)	57.1 (487)
White, % (n)	69.6 (55)	68.1 (111)	58.8 (251)	59.3 (506)
%BSA				
Mean (SD)	21.5 (18.2)	23.4 (20.9)	17.5 (17.1)	17.4 (17.3)
Median (min, max)	17.0 (5, 86)	15.0 (5, 95)	11.0 (5, 90)	10.0 (5, 95)
ISGA, % (n)				
Mild (2)	34.2 (27)	38.7 (63)	38.9 (166)	38.7 (330)
Moderate (3)	65.8 (52)	61.4 (100)	61.1 (261)	61.3 (523)
SPS, % (n)				
None (0)	1.3 (1)	5.5 (9)	4.2 (18)	3.1 (26)
Mild (1)	19 (15)	21.5 (35)	24.4 (104)	22.7 (194)
Moderate (2)	36.7 (29)	32.5 (53)	32.3 (138)	32.6 (278)
Severe (3)	29.1 (23)	32.5 (53)	26.5 (113)	29.9 (255)
Prior use of systemic corticosteroids,[a] % (n)	53.2 (42)	42.3 (69)	30.7 (131)	28.4 (242)
With asthma	62.8 (27/43)	52.8 (38/72)	41.8 (41/98)	40.9 (76/186)
Without asthma	41.7 (15/36)	34.1 (31/91)	27.4 (90/329)	24.9 (166/667)
Concurrent use of antihistamines, % (n)	53.2 (42)	38.7 (63)	21.6 (92)	21.3 (182)
With asthma	60.5 (26/43)	44.4 (32/72)	27.6 (27/98)	36.6 (68/186)
Without asthma	44.4 (16/36)	34.1 (31/91)	19.8 (65/329)	17.1 (114/667)

[a]Within 90 days before starting study treatment.

Efficacy

- The proportion of patients achieving ISGA success at day 29 was significantly greater in crisaborole-treated patients than in those receiving vehicle, regardless of past medical history of allergic rhinitis (**Figure 1**)
- Similarly, a significantly greater proportion of crisaborole-treated patients achieved ISGA clear or almost clear at day 29 than patients given vehicle (**Figure 2**)
- Improvement in SPS score at week 4 occurred in significantly more crisaborole- than vehicle-treated patients, irrespective of past medical history of allergic rhinitis (**Figure 3**)

Figure 1. Proportion of Patients Who Achieved ISGA Success[a] at Day 29



[a]ISGA success is defined as an ISGA of clear or almost clear with ≥2-grade improvement from baseline.

Figure 2. Proportion of Patients Who Achieved ISGA Clear or Almost Clear at Day 29

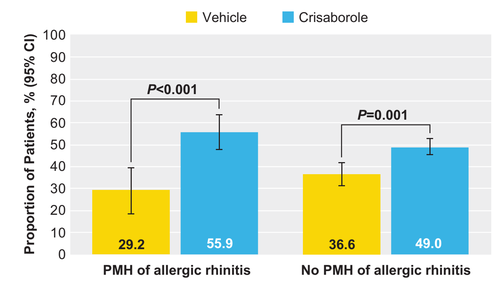
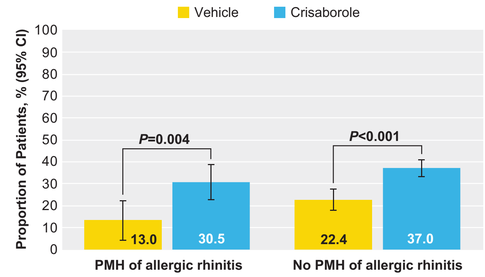


Figure 3. Proportion of Patients Who Experienced Improvement in SPS[a] at Week 4



[a]Improvement in SPS defined as weekly average SPS score ≤1 point with a ≥1-point improvement from baseline.

Safety

- The safety profile was generally similar between patients with allergic rhinitis and those without allergic rhinitis
- Among patients with allergic rhinitis, 53 crisaborole-treated patients (32.5%) and 22 vehicle-treated patients (27.8%) experienced at least 1 all-cause TEAE
- Among crisaborole-treated patients with allergic rhinitis, 34 patients (20.9 %) experienced a mild TEAE, 16 patients (9.8%) experienced a moderate TEAE, and 3 patients (1.8%) experienced a severe TEAE
- Individual TEAEs were infrequent (**Table 2**)
- The most common treatment-related TEAE in those with allergic rhinitis and in those without allergic rhinitis (crisaborole vs vehicle) was application site pain (4.9% vs 1.3% and 4.4% vs 1.2%, respectively)
- 1 crisaborole-treated patient with allergic rhinitis experienced a serious TEAE (pneumonia, 0.6%), and none treated with vehicle experienced a serious TEAE (0%); the serious TEAE was not considered treatment related
- Allergic rhinitis was reported as an AE in ≤2 patients in any group; no anaphylaxis was reported in any group

Table 2. Most Common (in >2% patients) TEAEs (all cause) in Patients With and Patients Without Allergic Rhinitis

	PMH of Allergic Rhinitis		No PMH of Allergic Rhinitis	
	Vehicle n=79	Crisaborole n=163	Vehicle n=420	Crisaborole n=849
AE (all cause), % (n)				
Application site pain	1.3 (1)	4.9 (8)	1.2 (5)	4.4 (37)
Upper respiratory tract infection	3.8 (3)	6.1 (10)	3.3 (14)	2.8 (24)
Viral upper respiratory tract infection	3.8 (3)	0.6 (1)	1.9 (8)	2.9 (25)
Pyrexia	2.5 (2)	1.2 (2)	1.4 (6)	2.6 (22)
Cough	0	0.6 (1)	2.1 (9)	1.8 (15)
Vomiting	0	2.5 (4)	1.2 (5)	1.5 (13)
TEAEs of special interest, % (n)				
Allergic rhinitis	0	1.2 (2)	0.2 (1)	0.1 (1)
Anaphylaxis	0	0	0	0

Limitations

- These post hoc analyses were not powered to detect treatment differences in allergic rhinitis subgroups
- The original studies were not specifically designed to evaluate the effects of crisaborole on allergic rhinitis

CONCLUSIONS

- **Regardless of whether patients have allergic rhinitis, crisaborole is effective in treating mild-to-moderate AD symptoms, including itch**
- **The safety profile was generally similar between patients with allergic rhinitis and those without allergic rhinitis, and no new safety signals were observed**
- **Crisaborole should be considered for the management of AD in patients whether or not the patients have concurrent allergic rhinitis**

Abbreviations **%BSA**, percentage of treatable body surface area; **AD**, atopic dermatitis; **AE**, adverse event; **ISGA**, Investigator's Static Global Assessment; **PDE4**, phosphodiesterase 4; **PMH**, past medical history; **SPS**, Severity of Pruritus Score; **TEAE**, treatment-emergent adverse event.

References **1.** Dharmage SC et al. *Allergy.* 2014;69:17-27. **2.** Silverberg JI. *Ann Allergy Asthma Immunol.* 2019;123:144-151. **3.** Silverberg JI. *Clin Dermatol.* 2017;35:360-366. **4.** Eucrisa (crisaborole) ointment, 2%, for topical use [package insert]. New York, NY: Pfizer Labs; April 2020. **5.** Paller AS et al. *J Am Acad Dermatol.* 2016;75:494-503.e496. **6.** Hanifin JM, Rajka G. *Acta Derm Venereol.* 1980;60:44-47. **7.** Yosipovitch G et al. *Itch.* 2018;3:e13.

This study was sponsored by Pfizer Inc.