Safety, Efficacy, and Pharmacokinetics (PK) of Crisaborole Ointment, 2%, in Infants Aged 3 to <24 Months With Mild-to-Moderate Atopic Dermatitis (AD)

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Presented at the American Academy of Dermatology 2020 Annual Meeting; March 20-24, 2020; Denver, Colorado

Disclosures and Acknowledgments

Disclosures

JS has received grants/research funding for his role as an investigator for Pfizer Inc., AbbVie, Aclaris, Allergan, Athenex, Brickell, Celgene, Croma-Pharma, Cutanea, Dr. Reddy's Laboratory, Eli Lilly, Endo Pharmaceuticals, Foamix, Galderma, Hovione, LEO Pharma, Menlo Therapeutics, Novartis, Prollenium, Qurient, Revance, Teoxane, UCB, and Vanda Pharmaceuticals; has received honoraria for serving on advisory boards for Allergan, Alphaeon, Bausch Health (Valeant), Galderma, and Revance; and is a stockholder of Allergan, Aclaris, Bausch Health (Valeant),and Revance. JSS was compensated as a principal investigator for this study, was compensated to serve on an advisory board for Pfizer Inc., and was compensated as a principal investigator for GSK, Incyte, and Merck. RG has received research grants for Pfizer crisaborole clinical trials and consulting fees for participating in the Pfizer crisaborole advisory board, as well as research grants from LEO Pharma and Incyte as an investigator. JCS has received grants/research funding for his role as an investigator for Pfizer Inc., AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pierre Fabre, and Sanofi; has received honoraria for serving on advisory boards for Pfizer Inc., Eli Lilly, GSK, Janssen, L'Oréal, Novartis, and Sanofi; and has received honoraria for serving as a speaker for Ego Pharmaceuticals and Pierre Fabre. CL has served as a principal investigator, consultant, and/or speaker for Pfizer Inc., AbbVie, Bausch Health (Valeant), Celgene, Eli Lilly, Janssen, LEO Pharma, and Novartis. AC, VP, LT, JLW, CZ, and BV are employees and stockholders of Pfizer Inc. WCP was an employee of Pfizer Inc. at the time of this study and is a stockholder of Pfizer Inc.

Acknowledgments

Editorial/medical writing support under the guidance of the authors was provided by Robert Schoen, PharmD, and Jennifer C. Jaworski, MS, 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).
This study was funded by Pfizer Inc.

Introduction, Objectives, Methods, and Baseline Characteristics

Introduction

- Crisaborole is a topical nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate AD[a]
- Crisaborole has not previously been studied in patients aged <2 years

Objectives

- Evaluate safety, efficacy, and PK profile of crisaborole in infants aged 3 to <24 months

Methods

- CrisADe CARE 1 (NCT03356977) is a multicenter, open-label, single-arm, phase 4 trial of crisaborole BID for 28 days[b]

Key Eligibility Criteria (all patients)	Additional PK Cohort-Specific Criteria
• Aged 3 to <24 months • Diagnosis of AD per Hanifin and Rajka criteria • Mild (2) or moderate (3) AD per ISGA • %BSA ≥5 (excluding scalp)	• ≥3 patients aged 3 to <9 months • Moderate (3) AD per ISGA • %BSA ≥35 (excluding scalp) • Adequate venous access for PK sampling • No lesions below wrists and below ankles or <2 cm from mouth

Baseline Characteristics

	Total N=137	PK Cohort N=21
Age, median (range), months	13.0 (3-23)	13.0 (3-23)
Male, n (%)	88 (64.2)	13 (61.9)
White, n (%)	84 (61.3)	13 (61.9)
ISGA, n (%)[c]		
Mild (2)	52 (38.0)	0
Moderate (3)	84 (61.3)	20 (95.2)
EASI score, mean (SD)	11.8 (8.4)	19.8 (4.4)
%BSA, mean (SD)	28.1 (22.0)	53.5 (12.6)
POEM total score, mean (SD)	14.8 (6.1)	19.7 (5.2)
Time since AD onset, mean (SD), months	10.2 (6.3)	9.1 (5.5)
History of other atopic conditions, n (%)	22 (16.1)	1 (4.8)
Prior medications, n (%)[d]		
TCS	72 (52.6)	9 (49.2)
TCI	2 (1.5)	0

%BSA, percentage of treatable body surface area; AD, atopic dermatitis; BID, twice daily; ISGA, Investigator's Static Global Assessment; PK, pharmacokinetic; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.
[a]Crisaborole is currently approved for patients aged ≥2 years.
[b]PK cohort dosed day 1 through the day 8 morning dose on site by staff and dosed at home post day 8 morning dose.
[c]1 patient had severe ISGA at baseline, which was a protocol deviation.
[d]Within 30 days of screening.

Safety Results

Overall TEAEs Reported for ≥3% of Patients

n (%)	N=137	
	All Cause	Treatment Related
Pyrexia	13 (9.5)	0
Upper respiratory tract infection	10 (7.3)	1 (0.7)
Diarrhea	10 (7.3)	0
Dermatitis atopic[a]	9 (6.6)	0
Dermatitis diaper	9 (6.6)	0
Cough	7 (5.1)	0
Otitis media	6 (4.4)	1 (0.7)
Eczema[a]	5 (3.6)	2 (1.5)
Application site pain	5 (3.6)	5 (3.6)
Conjunctivitis	5 (3.6)	0
Rhinorrhea	5 (3.6)	0

Treatment Area AEs Reported for ≥1.5% of Patients

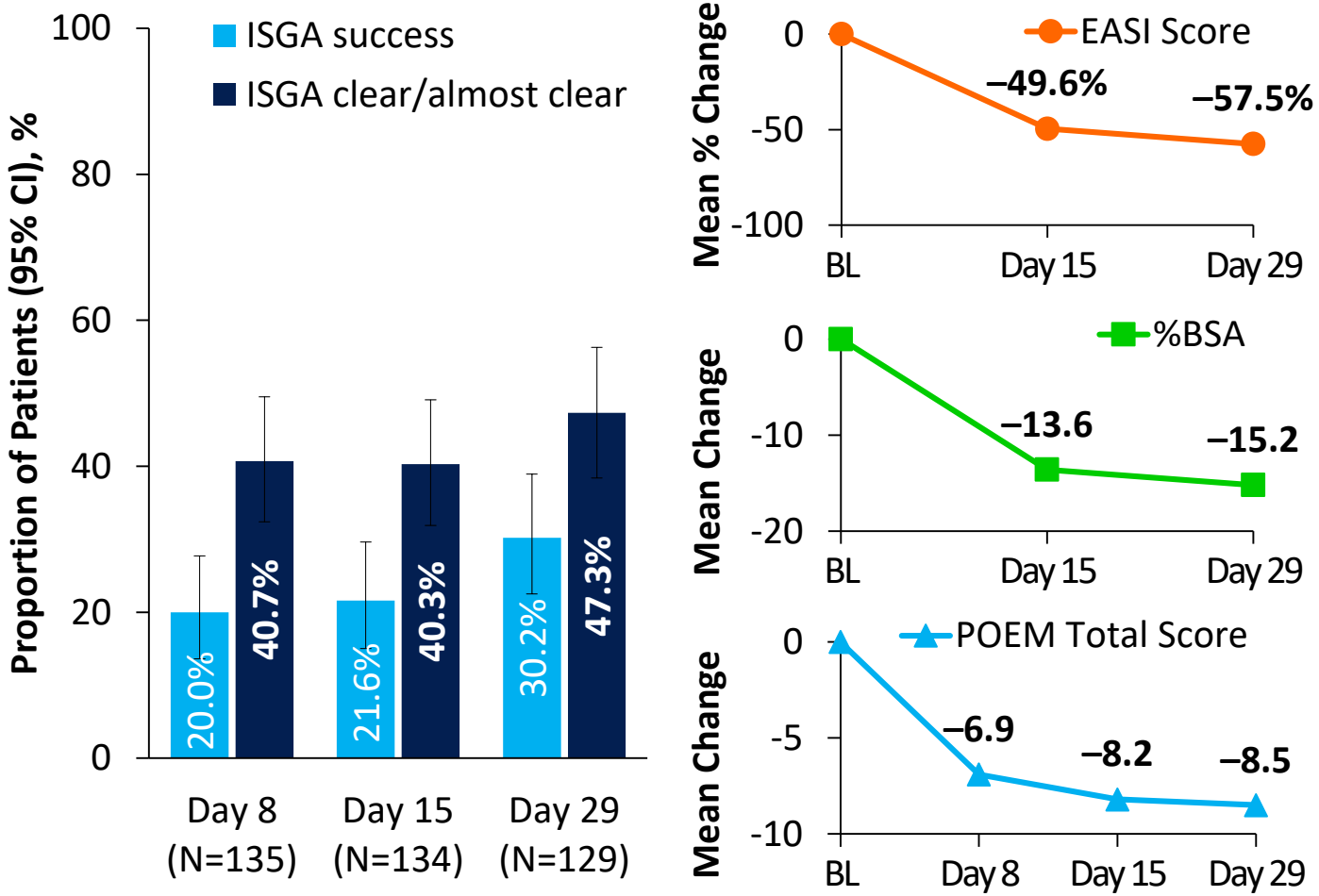
n (%)	N=137	
	All Cause	Treatment Related
Dermatitis atopic[a]	8 (5.8)	0
Application site pain	5 (3.6)	5 (3.6)
Eczema[a]	5 (3.6)	2 (1.5)
Application site discomfort	4 (2.9)	4 (2.9)
Erythema	4 (2.9)	4 (2.9)
Application site erythema	4 (2.9)	3 (2.2)
Dermatitis contact	4 (2.9)	1 (0.7)
Dermatitis diaper	4 (2.9)	0
Rash	4 (2.9)	0
Pruritus	3 (2.2)	3 (2.2)
Application site reaction	2 (1.5)	2 (1.5)
Rash pustular	2 (1.5)	0

- 4 (2.9%) patients discontinued treatment because of a TEAE and remained in the study, including:
  - 2 patients with TEAEs not related to treatment: 1 patient who experienced a serious TEAE of “febrile convulsion” and 1 patient with “dermatitis infected”
  - 2 patients with TEAEs considered treatment-related: 1 patient with “application site pain” and 1 patient with “application site discomfort”

AE, adverse event; TEAE, treatment-emergent adverse event.
[a]“Dermatitis atopic” or “eczema” may have been AD worsening/flare or a new AD lesion.

Efficacy and PK Results and Conclusions

Efficacy



Steady State PK (Day 8)[a]

Parameter, mean (SD)	Evaluable PK Cohort (N=16)[b]
C_{max}, ng/mL	315.7 (298.02)
AUC_{tau}, h·ng/mL	2021 (1867.1)
T_{max}, h	3.5 (2.2)

Conclusions

- Crisaborole was well tolerated and effective in infants aged 3 to <24 months with mild-to-moderate AD, with systemic exposures that were similar to those reported for patients ≥2 years of age[1-4]
- Treatment-related application site pain/discomfort incidence was similar to that in previous studies in patients aged ≥2 years (4.4%[1])

%BSA, percentage of treatable body surface area; AUC_{tau} area under concentration-time curve for a dosing interval; BL, baseline; C_{max} maximum concentration; EASI, Eczema Area and Severity Index; ISGA, Investigator's Static Global Assessment; PK, pharmacokinetic; POEM, Patient-Oriented Eczema Measure; T_{max}, time required to reach maximum concentration.
ISGA success defined as clear (0) or almost clear (1) with ≥2-grade improvement from baseline.
[a]PK cohort dosed day 1 through the day 8 morning dose on site by staff and dosed at home post day 8 morning dose.
[b]18 patients were evaluated for PK parameters. 2 additional patients were excluded because their postdose PK profiles were not consistent with the known PK characteristics of crisaborole, and study protocol deviations were confirmed (venipuncture site−treatment area overlap and venipuncture site cleaning procedures not followed), potentially resulting in PK sample contamination.
1. Paller AS et al. *J Am Acad Dermatol*. 2016;75:494-503.e6. 2. Zane LT et al. *Pediatr Dermatol*. 2016;33(4):380-387. 3. Purohit V et al. Presented at 2019 ACCP Annual Meeting; September 15-17, 2019; Chicago, Illinois. Poster 080. 4. Tom WL et al. *Pediatr Dermatol*. 2016;33(2):150-159.