CLINICAL STUDY REPORT SYNOPSIS

Sponsor: Pfizer Inc.

Investigational Product: PF-06930164

Clinical Study Report Synopsis: Protocol C3291032

Protocol Title: A Phase 3, Multicenter, Randomized, Double Blind, Vehicle Controlled Study of the Efficacy and Safety of Crisaborole Ointment, 2% in Chinese and Japanese Pediatric and Adult Subjects (Ages 2 Years and Older) With Mild to Moderate Atopic Dermatitis

Investigators: Refer to Appendix 16.1.4.1 for a list of investigators involved in this study.

Study Centers: Refer to Appendix 16.1.4.1 for a list of sites involved in this study.

Publications Based on the Study: None

Study Initiation Date: 27 July 2020

Study Completion Date: 08 September 2021

Report Date: 17 January 2022

Previous Report Date: Not Applicable

Phase of Development: Phase 3

Primary and Secondary Study Objectives and Endpoints:

Primary and secondary objectives and endpoints are presented in Table S1.

Table S1. Study Primary and Secondary Objectives and Endpoints

Type	Objective	Endpoint
Primary		
Efficacy	To evaluate the efficacy of crisaborole ointment, 2% applied twice daily (BID) versus vehicle in Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate atopic dermatitis (AD).	Percent change from baseline in Eczema Area and Severity Index (EASI) total score at Day 29.
Safety	To evaluate the safety and tolerability of crisaborole ointment, 2% applied BID versus vehicle in Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate AD.	Treatment-emergent adverse events (TEAEs) (including application site reactions), serious adverse events (SAEs) and clinically significant changes in vital signs and clinical laboratory parameters.

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Table S1. Study Primary and Secondary Objectives and Endpoints

Type	Objective	Endpoint
Secondary		
Efficacy	• To evaluate the effect of crisaborole ointment, 2% applied BID versus vehicle on additional efficacy endpoints in Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate AD. • To evaluate the effect of crisaborole ointment, 2% applied BID versus vehicle on patient/observer reported outcomes over time in Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate AD.	Key secondary efficacy endpoints. • Achievement of improvement in Investigator's Static Global Assessment (ISGA) (defined as ISGA score of Clear [0] or Almost Clear [1]) at Day 29. • Achievement of success in ISGA (defined as an ISGA score of Clear [0] or Almost Clear [1] with at least a 2-grade improvement from Baseline) at Day 29. • Change from baseline in Peak Pruritus Numeric Rating Scale (PP-NRS) at Week 4 - for participants ≥12 years. Other secondary efficacy endpoints: • Success in ISGA over time. • Improvement in ISGA over time. • Percent change from baseline in EASI total score over time. • Change from baseline in percent body surface area (%BSA) over time. • Achievement of EASI-50 (≥50% improvement from baseline) over time. • Achievement of EASI-75 (≥75% improvement from baseline) over time. • Change from baseline in PP-NRS over time - for participants ≥12 years. • Change from baseline in Patient Reported Itch Severity Scale over time - for participants ≥6 years and <12 years. • Change from baseline in Observer Reported Itch Severity Scale over time - for participants <6 years. • Dermatology Life Quality Index (DLQI), Children'S Dermatology Life Quality Index

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Table S1. Study Primary and Secondary Objectives and Endpoints

Type	Objective	Endpoint
		(CDLQI), Infants' Dermatitis Quality of Life Index (IDQOL), Dermatitis Family Impact Questionnaire (DFI), Patient Oriented Eczema Measure (POEM), Patient Global Impression of Severity (PGIS)/Observer Global Impression of Severity (OGIS), Patient Global Impression of Change (PGIC)/Observer Global Impression of Change (OGIC) over time.

METHODS

Study Design:

This was a Phase 3, multicenter, randomized, double-blind, vehicle-controlled study to evaluate the efficacy and safety of crisaborole ointment, 2% in Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate AD involving at least 5% treatable BSA.

A total of approximately 384 participants (approximately 50% for age ≥12 years old and approximately 50% for age <12 years old) were to be enrolled in the study from multiple sites in China and Japan. Following the screening period (up to 35 days prior to Baseline/Day 1), eligible participants were randomized at the Baseline/Day 1 visit in a 2:1 ratio to one of 2 treatment groups (crisaborole ointment, 2% BID; vehicle BID, respectively), the investigational product was applied BID for 28 days to the treatable BSA identified at Baseline/Day 1 and new AD lesions that appeared after the Baseline/Day 1. The primary efficacy endpoint, percent change from baseline in EASI total score, was assessed at Day 29.

Scheduled study visits for all participants occurred at Screening, Baseline/Day 1, Day 8, Day 15, Day 22, Day 29 (End of treatment/Early termination). A follow-up telephone call was made by site staff to the participants and/or parents/legal guardians on Day 36 and Day 60.

Japan participants who rolled over into Study C3291027 without a Post-Treatment Follow Up period prior to 21 Oct 2020 were considered completers in this study.

Diagnosis and Main Criteria for Inclusion: Chinese and Japanese pediatric and adult participants (ages 2 years and older) with mild to moderate AD involving at least 5% treatable BSA were enrolled in the study.

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Study Treatment:

Crisaborole ointment, 2% was for external use on the skin only. Ointment was applied as an even layer of approximately 3 mg/cm^2, based on each participant's own AD %BSA adjusted by height and weight.

Investigational product was applied BID to all treatable AD involved areas (excluding the scalp) identified at Baseline/Day 1 through Day 28.

Crisaborole ointment, 2% and vehicle ointment were supplied in 60 g tubes for topical administration. The tubes were provided in cartons and labeled in a blinded fashion according to local regulatory requirements.

Investigational product description is provided in Table S2.

Table S2. Investigational Product Description

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/Potency	Dosage Form
Placebo for Crisaborole Topical Ointment in 60 g Tube (Axomatic)	K190622D	19-002899	0 mg/g	Ointment
Crisaborole 2% Topical Ointment in 60 g Tube	K062518D	19-000158	20 mg/g	Ointment
Placebo for Crisaborole Topical Ointment in 60 g Tube (Axomatic)	K121917D	18-000180	0 mg/g	Ointment

Efficacy Evaluations:

Calculation of Participant's Treatable % BSA

Treatable %BSA was defined as the percentage of the participant's total BSA that was AD involved, excluding the scalp. To estimate the participant's treatable %BSA, the investigator or his/her designee used "handprint method", by which the area represented by the palmar (ie, outstretched) surface of the participant's hand with all 5 digits adducted together was approximately 1% of the participant's BSA, regardless of the participants age.

Eczema Area and Severity Index (EASI)

The EASI quantified the severity of a participant's AD based on both severity of lesion clinical signs and the percent of BSA affected. EASI was a composite scoring of the degree of erythema, induration/papulation, excoriation, and lichenification (each scored separately) for each of 4 body regions, with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole body.

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Investigator's Static Global Assessment (ISGA)

ISGA was a five-point global static assessment of AD severity. ISGA was assessed to characterize participants' overall disease severity across all treatable AD lesions. The assessment was a static evaluation without regard to the score at a previous visit.

Patient/Observer Reported Outcomes

The Patient/Observer Reported Outcomes questionnaires in this study included: PP-NRS/Patient Reported Itch Severity Scale/Observer Reported Itch Severity Scale, PGIS/OGIS, PGIC/OGIC, POEM, DLQI, CDLQI, IDQOL, and DFI.

Pharmacokinetic, Pharmacodynamic, Pharmacogenomic, and/or Other Evaluations:
Not Applicable.

Safety Evaluations:

Safety evaluations included AEs, vital signs, and safety laboratory tests.

Statistical Methods:

Efficacy

The study was supposed to be declared a success with crisaborole shown to be superior to vehicle with respect to the primary efficacy endpoint, percent change from baseline in EASI total score at Day 29, if the mean percent change in the crisaborole arm was lower than that in the vehicle arm and the difference was statistically significant at the two-sided level of 0.05.

The primary efficacy endpoint, percent change from baseline in EASI total score at Day 29, was analyzed using a linear mixed-effect model for repeated measures that included treatment group, visit, and treatment group-by-visit interaction as factors and baseline value as a covariate. Within-participant variability was accounted for using a random effect with the first-order autoregressive (AR[1]) covariance matrix.

For the key secondary efficacy endpoints, the percentages of participants with Improvement in ISGA at Day 29 and Success in ISGA at Day 29 were compared between crisaborole arm and vehicle arm and the difference was tested based on normal approximation to response rates. Missing Day 29 ISGA scores was derived for the analysis using the method of multiple imputations (MI) based on Markov Chain Monte Carlo (MCMC). The change from baseline to Week 4 in weekly average of PP-NRS was analyzed using a linear mixed-effect model for repeated measures that includes treatment group, visit, and treatment-group-by-visit interaction as factors and baseline value as a covariate.

Other secondary efficacy endpoints including change from Baseline in % BSA, percent change from baseline in EASI total score at all time points other than Day 29, change from

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baseline in weekly average of PP-NRS of weeks other than Week 4, change from baseline in weekly average of Patient Reported Itch Severity Scale, and change from baseline in weekly average of Observer Reported Itch Severity Scale were analyzed similarly as the primary efficacy endpoints using a linear mixed effect model for repeated measures.

Other secondary efficacy endpoints including EASI-50 and EASI-75 at all timepoints, as well as Success in ISGA and Improvement in ISGA at all time points other than Day 29, were analyzed using normal approximation to response rates.

DLQI, CDLQI, IDQOL, DFI, POEM, PGIS/OGIS, and PGIC/OGIC were summarized descriptively, missing values were handled as per the SAP.

Safety

Safety data were descriptively summarized and were presented in tabular. No imputation was made for missing safety data. The following safety data were summarized:

- TEAEs, including SAEs;
- Clinically significant changes in vital signs;
- Clinically significant changes in laboratory parameters.

RESULTS

Participant Disposition and Demography:

Participant disposition is presented graphically in Figure S1. Of 418 participants screened for this study, 391 were assigned to treatment. All the 391 participants were treated including 131 participants in the vehicle group and 260 in the crisaborole 2% BID group. A total of 345 (88.2%) participants completed follow-up.

- During the double-blind treatment phase, participant discontinuation rate was higher in the vehicle group (17.6%) compared with the crisaborole 2% BID group (5.8%). The most common reason was AE (6.9% and 4.2% in the vehicle and crisaborole 2% BID groups, respectively).
- The proportion of participants completing the double-blinded treatment period was 82.4% in the vehicle group and 94.2% in the crisaborole 2% BID group.
- During the follow-up phase, only 1 (0.3%) participant in the vehicle group discontinued.
- The proportion of participants completing the follow-up phase was comparable between the vehicle group and the crisaborole 2% BID group.

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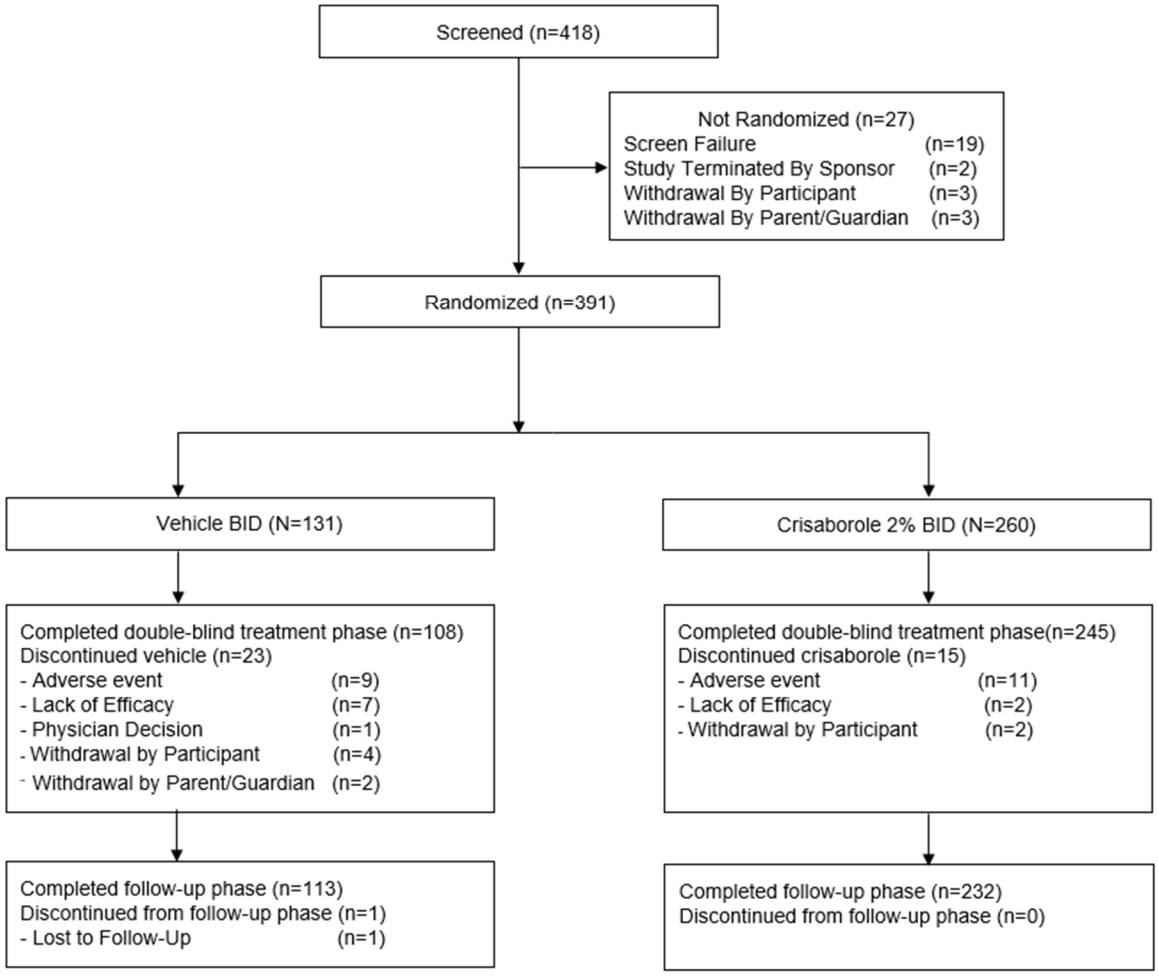
Figure S1. Participant Disposition



Baseline demographic characteristics were balanced between the vehicle and crisaborole 2% BID groups.

- The mean age was 16.0 and 19.4 years in the vehicle and crisaborole 2% BID groups, respectively; overall approximately 50% for age ≥12 years old and approximately 50% for age <12 years old were enrolled in the study as planned.

- Overall, 60.6% of the participants were from China and 39.4% were from Japan.

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Efficacy Results:

Primary Endpoint Result

Statistically significantly greater reduction in percent change from baseline in EASI total score was observed for participants in the crisaborole 2% BID group at Day 29 compared to the vehicle group, with LSM difference of -17.13% and p-value of 0.0002 (Table S3).

Table S3. Least Square Mean of Percent Change from Baseline in EASI Total Score at Day 29 - MMRM - Main Analysis (FAS, OC) (Protocol C3291032)

Analysis Visit		Vehicle BID (N=131)	Crisaborole 2% BID (N=260)
	n	124	256
Day 29	LSM	-42.79	-59.92
	95% CI	(-50.14, -35.44)	(-64.86, -54.98)
	Active - Vehicle		
	LSM Difference		-17.13
	95% CI		(-25.98, -8.27)
	Two-sided P-value		0.0002

N: Number of participants in the full analysis set population. n: Number of participants included in the analysis model.
Mixed Model Repeated Measure (MMRM) contained treatment group, visit, treatment group by visit interaction as factors and baseline value as a covariate.
Within-participant variability was accounted for using a random effect with the first order autoregressive (AR(1)) covariance matrix.
Data after treatment discontinuation was not considered.
PFIZER CONFIDENTIAL SDTM Creation: 07OCT2021 (21:32) Source Data: adea Table Generation: 19OCT2021 (04:19)
(Data cutoff date : 01Oct2021 Database snapshot date : 01Oct2021) Output File: ./nda1_cdisc/C3291032_CSR/adea_s101 Table 14.2.1.2.1.1.1 Crisaborole is for Pfizer internal use.

Key Secondary Endpoints Results

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The proportion of participants achieving improvement in ISGA (defined as ISGA score of Clear [0] or Almost Clear [1]) at Day 29 in the crisaborole 2% BID group was statistically significantly higher than that in the vehicle group, with response difference of 12.9% and p-value of 0.0124 (Table S4).

Table S4. Achievement of Improvement in ISGA at Day 29 - Main Analysis (FAS, MI-MCMC) (Protocol C3291032)

Analysis Visit		Vehicle BID (N=131)	Crisaborole 2% BID (N=260)
	n	131	260
Day 29	Response (%)	28.5	41.4
	95% CI	(20.4, 36.6)	(35.4, 47.5)
	Active - Vehicle		
	Response Difference		12.9
	95% CI		(2.8, 23.1)
	Two-sided P-value		0.0124

N: Number of participants in the full analysis set population. n: Number of participants included in the analysis model.
Improvement was defined as ISGA score of clear (0) or almost clear (1).
Data after treatment discontinuation was not considered.
The difference was tested based on normal approximation to response rates.
PFIZER CONFIDENTIAL SDTM Creation: 07OCT2021 (22:07) Source Data: adadmi Table Generation: 19OCT2021 (04:24)
(Data cutoff date : 01Oct2021 Database snapshot date : 01Oct2021) Output File: ./nda1_cdisc/C3291032_CSR/adad_s101 Table 14.2.2.1.2.1 Crisaborole is for Pfizer internal use.

The proportion of participants achieving success in ISGA (defined as an ISGA score of Clear [0] or Almost Clear [1] with at least a 2-grade improvement from baseline) at Day 29 in the crisaborole 2% BID group was statistically significantly higher than that in the vehicle group (response difference: 11.7%; p=0.0078) (Table S5).

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Table S5. Achievement of Success in ISGA at Day 29 for Participants with Baseline Values ≥2 - Main Analysis (FAS, MI-MCMC) (Protocol C3291032)

Analysis Visit		Vehicle BID (N=131)	Crisaborole 2% BID (N=260)
	n	131	260
Day 29	Response (%)	15.9	27.6
	95% CI	(9.4, 22.5)	(22.1, 33.1)
	Active - Vehicle		
	Response Difference		11.7
	95% CI		(3.1, 20.3)
	Two-sided P-value		0.0078

N: Number of participants in the full analysis set population with the baseline values ≥2. n: Number of participants included in the analysis model with the baseline values ≥2.
Success was defined as an ISGA score of Clear (0) or Almost Clear (1) with at least a 2-grade improvement from Baseline.
Data after treatment discontinuation was not considered.
The difference was tested based on normal approximation to response rates.
PFIZER CONFIDENTIAL SDTM Creation: 07OCT2021 (22:07) Source Data: adadmi Table Generation: 19OCT2021 (04:37)
(Data cutoff date : 01Oct2021 Database snapshot date : 01Oct2021) Output File: ./nda1_cdisc/C3291032_CSR/adad_s201 Table 14.2.2.2.2.1 Crisaborole is for Pfizer internal use.

Statistically significantly greater reduction in change from baseline in PP-NRS was observed at Week 4 for participants ≥12 years in the crisaborole 2% BID groups, compared to the vehicle group (least square mean [LSM] difference: -0.79; p-value=0.0009) (Table S6).

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Table S6. Least Square Mean of Change from Baseline in Weekly Average of PP-NRS at Week 4 (Participants ≥12 Years) - MMRM - Main Analysis (FAS, OC) (Protocol C3291032)

Analysis Visit		Vehicle BID (N=62)	Crisaborole 2% BID (N=137)
	n	60	131
Week 4	LSM	-0.79	-1.58
	95% CI	(-1.18, -0.40)	(-1.84, -1.33)
	Active - Vehicle		
	LSM Difference		-0.79
	95% CI		(-1.26, -0.33)
	Two-sided P-value		0.0009

N: Number of participants with ≥12 years old in the full analysis set population. n: Number of participants included in the analysis model.
Mixed Model Repeated Measure (MMRM) contained treatment group, visit, treatment group by visit interaction as factors and baseline value as a covariate.
Within-participant variability was accounted for using a random effect with the first order autoregressive (AR(1)) covariance matrix.
Data after treatment discontinuation was not considered.
PFIZER CONFIDENTIAL SDTM Creation: 07OCT2021 (22:07) Source Data: adnr Table Generation: 19OCT2021 (04:32)
(Data cutoff date : 01Oct2021 Database snapshot date : 01Oct2021) Output File: ./nda1_cdisc/C3291032_CSR/adnr_s101 Table 14.2.3.2.1.1 Crisaborole is for Pfizer internal use.

Other Secondary Endpoints Results

ISGA: The proportions of participants who achieved ISGA success at all timepoints (Days 8, 15, 22 and 29) in the crisaborole 2% BID group were higher compared to the vehicle group. Similar results were observed in ISGA improvements at all timepoints.

EASI: LSM of decrease in percent change from baseline in EASI total score in the crisaborole 2% BID group was greater compared to the vehicle group over time. Higher proportion of participants in the crisaborole 2% BID group achieving EASI-50 response was observed, compared to the vehicle group at all timepoints. Similar results were observed in EASI-75 response at all timepoints.

%BSA: LSM of decrease in change from baseline in %BSA affected was greater in the crisaborole 2% BID group, compared to the vehicle group over time.

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PP-NRS: LSM of decrease in change from baseline in PP-NRS was greater for participants ≥12 years in the crisaborole 2% BID group, compared to the vehicle group from Weeks 1 to 4.

Patient/Observer Reported Itch Severity Scale: For participants ≥6 years and <12 years, LSM of decrease in change from baseline in patient reported itch severity scale in the crisaborole 2% BID group was greater, compared to the vehicle group from Weeks 1 to 4. For participants <6 years, LSM of decrease in change from baseline in observer reported itch severity scale in the crisaborole 2% BID group was greater, compared to the vehicle group from Weeks 1 to 4.

PROs: Numerically greater reduction from baseline in DLQI, CDLQI, IDQOL, DFI, POEM, and PGIS/OGIS was observed in the crisaborole 2% BID group, compared to the vehicle group at all timepoints. Mean values of PGIC and OGIC in the crisaborole 2% BID group were numerically lower than that in the vehicle group at all timepoints.

Pharmacokinetic, Pharmacodynamic, Pharmacogenomic, Immunogenicity and/or Other Results: Not Applicable.

Safety Results:

AEs

The majority of all-causality TEAEs were mild or moderate in severity. The proportion of participants with all-causality TEAEs was similar between the vehicle and crisaborole 2% BID groups (44.3% and 46.2%, respectively). The proportion of participants with treatment-related AEs was 18.3% and 23.5% in the vehicle and crisaborole 2% BID groups, respectively. No deaths were reported in the study. All-causality SAEs were observed in 1 participant each in the vehicle and crisaborole 2% BID groups (0.8% and 0.4%, respectively); neither of the SAEs were treatment-related.

- The most frequently reported AEs regardless of causality in the vehicle and crisaborole 2% BID groups were application site pain (3.8% and 13.1%, respectively), dermatitis atopic (11.5% and 7.7%, respectively), folliculitis (4.6% and 3.1%, respectively), nasopharyngitis (3.1% and 3.5%, respectively), upper respiratory tract infection (3.1% and 3.5%, respectively) and application site discolouration (0.8% and 3.5%, respectively).

- The most frequently reported treatment-related AEs in the vehicle and crisaborole 2% BID groups were application site pain (3.8% and 13.1%, respectively), dermatitis atopic (4.6% and 2.3%, respectively), folliculitis (3.8% and 2.3%, respectively) and application site discolouration (0.8% and 3.1%, respectively).

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- There was only 1 participant discontinued from study due to AE. This participant was from the vehicle group at China site and discontinued from study due to a treatment-related moderate AE of dermatitis atopic.

- Eight (6.1%) and 11 (4.2%) participants discontinued from study treatment due to AEs and continued study in the vehicle and crisaborole 2% BID groups, respectively. Six (4.6%) and 8 (3.1%) participants discontinued from study treatment due to treatment-related AEs and continued study in the vehicle and crisaborole 2% BID groups, respectively.

- The proportion of participants with AEs associated with dose reduction was low (2 [0.8%] participants in the crisaborole 2% BID group and 1 [0.8%] in the vehicle group). Dose reduction means that study treatment was not used on all AE-impacted areas. No participants had AEs associated with temporary discontinuation in either treatment group.

- The proportion of participants with AEs of application site reaction in the crisaborole 2% BID group was higher than that in the vehicle group (all-causality: 20.4% versus 7.6%; treatment-related: 19.2% versus 6.9%). The most frequently reported AE in both treatment groups was application site pain (13.1% in the crisaborole 2% BID group and 3.8% in the vehicle group), all of which were considered treatment-related.

- All-causality SAEs were reported in 1 participant each in the vehicle and crisaborole 2% BID groups. In the crisaborole 2% BID group, 1 participant at China site experienced an AE of carpal tunnel syndrome on Study Day 17. No action was taken in response to this AE. An SAE of exacerbation of carpal tunnel syndrome was reported on Study Day 29 after end of treatment (MedDRA Low-Level Term [LLT] indicating carpal tunnel syndrome exacerbation is not available, so an additional preferred term condition aggravated was coded to reflect this per safety policy). The SAE resolved on Study Day 31. Neither of the events were considered treatment-related. In the vehicle group, 1 participant at China site experienced SAE of myocardial necrosis marker increased on Study Day 32. Concomitant medications including fructose diphosphate sodium, fructose diphosphate sodium and ascorbic acid were given in response to this event. The SAE resolved on Study Day 38. This SAE was considered not related to study treatment.

Clinical Laboratory Tests

Without regard to baseline abnormality, the proportion of participants with laboratory abnormalities was similar between the vehicle and crisaborole 2% BID groups (42.9% and 41.9%). The most frequently reported laboratory abnormalities were increased eosinophils (>1.2× upper limit of normal [ULN]) and increased eosinophils/leukocytes (>1.2×ULN) in both vehicle and crisaborole 2% BID groups.

Vital Signs and Physical Examination

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No clinically significant changes or pattern in vital sign or physical examination data occurred in either treatment group.

Conclusions:

The crisaborole 2% BID treatment met pre-specified statistical decision rules for the primary and key secondary efficacy endpoints, thus crisaborole showed statistical superiority to vehicle. The data (both efficacy and safety) are consistent with previous clinical trial experience with crisaborole. Crisaborole ointment 2% was effective and well-tolerated (no new safety signals were identified) in Chinese and Japanese participants ages 2 years and older with mild to moderate AD.

Efficacy

Crisaborole is shown to be statistically superior to vehicle with respect to the primary efficacy endpoint, percent change from baseline in EASI total score at Day 29, and key secondary efficacy endpoints - achievement of improvement in ISGA at Day 29, achievement of success in ISGA at Day 29 and the change from baseline in PP-NRS at Week 4 for participants ≥12 years.

- The study met its primary objective: statistically significant reduction in percent change from baseline in EASI total score was observed for participants in the crisaborole 2% BID group at Day 29 compared to vehicle, with LSM difference of -17.13% and p-value of 0.0002.

- The study met its key secondary objectives:

    - Improvement in ISGA at Day 29 was achieved in 41.4% of the participants in the crisaborole 2% BID group, which was statistically significantly higher, compared with 28.5% of the participants in the vehicle group (p=0.0124).

    - Success in ISGA at Day 29 was achieved in 27.6% of the participants in the crisaborole 2% BID group, which was statistically significantly higher, compared with 15.9% of the participants in the vehicle group (p=0.0078).

    - Statistically significantly greater reduction in PP-NRS was observed at Week 4 for participants ≥12 years in the crisaborole 2% BID groups, compared to the vehicle group (LSM difference: -0.79; p-value=0.0009).

- Other secondary efficacy endpoints (ISGA, EASI, %BSA, PP-NRS, patient and observer reported itch severity scales) demonstrated improved efficacy response in the crisaborole 2% BID group compared to the vehicle group over time.

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- The findings from Patient-Reported Outcomes (PROs) measures utilized in the study (DLQI, CDLQI, IDQOL, DFI, POEM, PGIS/OGIS, and PGIC/OGIC) were consistent with the primary and other secondary efficacy endpoints.

Safety

- Crisaborole ointment 2% was well-tolerated in Chinese and Japanese participants ages 2 years and older with mild to moderate AD. The observed safety events were consistent with those in other crisaborole studies. No new safety signals were identified.

- The safety profile was similar between the vehicle and crisaborole 2% BID groups.

    - No deaths were reported in this study.

    - The proportions of participants with SAEs, severe AEs and AEs leading to study discontinuation were low.

    - The majority of all-causality TEAEs were mild or moderate.

    - Application site pain was the most frequently reported TEAE in the crisaborole 2% BID group and the proportion of participants with application site pain was higher in the crisaborole 2% BID group than that in the vehicle group.

    - No safety signals were identified in laboratory or vital sign results.

- Crisaborole ointment 2% shows a positive benefit-risk profile for the treatment of mild to moderate AD in Chinese and Japanese participants aged 2 years and older.