EU Clinical Trials Register

Clinical trial results:
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

Summary

EudraCT number	2021-006538-38
Trial protocol	Outside EU/EEA
Global end of trial date	08 September 2021

Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022

Trial information

Trial identification

Sponsor protocol code	C3291032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04360187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 September 2021
Global end of trial reached?	Yes
Global end of trial date	08 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate 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 involving at least 5% treatable body surface area (BSA).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed. The external data monitoring committee (E-DMC) was responsible for ongoing monitoring of the safety of subjects in the study according to the charter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 237
Country: Number of subjects enrolled	Japan: 154
Worldwide total number of subjects	391
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	192
Adolescents (12-17 years)	40
Adults (18-64 years)	154
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

418 subjects were screened, 391 of whom were randomized and treated.

Period 1

Period 1 title	Double-Blind Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Vehicle Twice a Day (BID)

Arm description:

Vehicle was applied BID for 28 days to the Treatable body surface area (BSA) identified at Baseline/Day 1 and new atopic dermatitis (AD) lesions that appear after the Baseline/Day 1.

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

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

Arm title	Crisaborole 2% Twice a Day (BID)

Arm description:

Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.

Arm type	Experimental
Investigational medicinal product name	Crisaborole 2%
Investigational medicinal product code	PF-06930164
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Crisaborole 2% was applied BID to all treatable AD involved areas (excluding the scalp) identified at Baseline/Day 1 through Day 28

Number of subjects in period 1	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)
Started	131	260
Completed	108	245
Not completed	23	15
Physician decision	1	-
Consent withdrawn by subject	4	2
Adverse event, non-fatal	9	11
Withdrawal By Parent/Guardian	2	-
Lack of efficacy	7	2

Period 2

Period 2 title	Follow-Up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Vehicle Twice a Day (BID)

Arm description:

Vehicle was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

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

Arm title	Crisaborole 2% Twice a Day (BID)

Arm description:

Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.

Arm type	Experimental
Investigational medicinal product name	Crisaborole 2%
Investigational medicinal product code	PF-06930164
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Crisaborole 2% was applied BID to all treatable AD involved areas (excluding the scalp) identified at Baseline/Day 1 through Day 28

Number of subjects in period 2[1]	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)
Started	114	232
Completed	113	232
Not completed	1	0
Lost to follow-up	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All subjects from double-blind treatment period did not enter into follow-up period.

Baseline characteristics

Reporting groups

Reporting group title	Vehicle Twice a Day (BID)
Reporting group description:	
Vehicle was applied BID for 28 days to the Treatable body surface area (BSA) identified at Baseline/Day 1 and new atopic dermatitis (AD) lesions that appear after the Baseline/Day 1.	
Reporting group title	Crisaborole 2% Twice a Day (BID)
Reporting group description:	
Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	

Reporting group values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)	Total
Number of subjects	131	260	391
Age Categorical			
Units: Subjects			
2-11 Years	69	123	192
12-17 Years	15	25	40
>=18 Years	47	112	159
Age continuous			
Units: years			
arithmetic mean	16.0	19.4	
standard deviation	± 13.58	± 15.80	-
Sex: Female, Male			
Units: Subjects			
Female	64	122	186
Male	67	138	205
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	131	260	391
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	131	260	391
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Vehicle Twice a Day (BID)
Reporting group description:	
Vehicle was applied BID for 28 days to the Treatable body surface area (BSA) identified at Baseline/Day 1 and new atopic dermatitis (AD) lesions that appear after the Baseline/Day 1.	
Reporting group title	Crisaborole 2% Twice a Day (BID)
Reporting group description:	
Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	
Reporting group title	Vehicle Twice a Day (BID)
Reporting group description:	
Vehicle was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	
Reporting group title	Crisaborole 2% Twice a Day (BID)
Reporting group description:	
Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	

Primary: Percent Change From Baseline in Eczema Area and Severity Index (EASI) Total Score at Day 29

End point title	Percent Change From Baseline in Eczema Area and Severity Index (EASI) Total Score at Day 29
End point description:	
The EASI quantifies the severity of a subject's atopic dermatitis (AD) based on both severity of lesion clinical signs and the percent of body surface area (BSA) affected. EASI is a composite scoring of the degree of erythema, induration/papulation, excoriation, and lichenification (each scored separately) for each of four 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. Total EASI score ranged from 0.0 to 72.0, higher scores = greater severity of AD. Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.	
End point type	Primary
End point timeframe:	
Baseline, Day 29	

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	256		
Units: Percent Change				
least squares mean (confidence interval 95%)	-42.79 (-50.14 to -35.44)	-59.92 (-64.86 to -54.98)		

Statistical analyses

Statistical analysis title	Crisaborole versus Vehicle
Comparison groups	Crisaborole 2% Twice a Day (BID) v Vehicle Twice a Day (BID)
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed effect Model for Repeated Measures
Parameter estimate	LS mean of difference
Point estimate	-17.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.98
upper limit	-8.27

Primary: Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)[1]

End point description:

An adverse event was considered as a treatment-emergent adverse event (TEAE) if the event started after the first dose of treatment regardless of whether a similar event of equal or greater severity existed in the baseline period. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs are classified according to the severity in 3 categories a) mild – AEs does not interfere with subject's usual function b) moderate – AEs interferes to some extent with subject's usual function c) severe – AEs interferes significantly with subject's usual function.
Overall number of subjects analyzed included all subjects who were randomized and received at least 1 confirmed dose of investigational product.

End point type	Primary

End point timeframe:

Baseline up to Day 60

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (not applicable)				
With Adverse Events (AEs)	44.3	46.2		
With Serious AEs	0.8	0.4		
With Severe AEs	1.5	0		
Discontinued (D/C) From Study due to AEs	0.8	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Clinically Significant Changes From Baseline in Clinical Laboratory Parameters

End point title	Percentage of Subjects With Clinically Significant Changes From Baseline in Clinical Laboratory Parameters[2]

End point description:

Laboratory parameters included: hematology and chemistry. Clinically significant laboratory abnormalities are defined as abnormal values that have clinical manifestations or require medical intervention. Clinically significant laboratory criteria included Hemoglobin <0.8 x lower limit of normal (LLN), Leukocytes >1.5 x upper limit of normal (ULN), Lymphocytes <0.8 x LLN, Lymphocytes/Leukocytes >1.2 x ULN, Neutrophils <0.8 x LLN, Neutrophils >1.2x ULN, Neutrophils/Leukocytes <0.8 x LLN, Basophils/Leukocytes >1.2 x ULN, Eosinophils >1.2 x ULN, Eosinophils/Leukocytes >1.2 x ULN, Monocytes >1.2 x ULN, Monocytes/Leukocytes (%) >1.2 x ULN, Bicarbonate <0.9 x LLN, and Glucose >1.5x ULN.
Overall number of subjects analyzed included all subjects who were randomized and received at least 1 confirmed dose of investigational product.

End point type	Primary

End point timeframe:

Baseline up to Day 29

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	258		
Units: Percentage of Subjects				
number (not applicable)				
Hemoglobin <0.8 x lower limit of normal (LLN)	1.6	0		
Leukocytes >1.5 x upper limit of normal (ULN)	0	0.4		
Lymphocytes <0.8 x LLN	0.8	0		
Lymphocytes/Leukocytes >1.2 x ULN	3.2	1.9		
Neutrophils <0.8 x LLN	0	0.4		
Neutrophils >1.2 x ULN	0	0.4		
Neutrophils/Leukocytes <0.8 x LLN	3.2	2.7		
Basophils/Leukocytes >1.2 x ULN	4.8	3.1		
Eosinophils >1.2 x ULN	33.1	31.1		
Eosinophils/Leukocytes >1.2 x ULN	29.8	33.1		
Monocytes >1.2 x ULN	0	0.4		
Monocytes/Leukocytes >1.2 x ULN	1.6	1.6		
Bicarbonate <0.9 x LLN	0.8	0.8		
Glucose >1.5 x ULN	0	0.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Clinically Significant Changes From Baseline in Vital Signs

End point title	Percentage of Subjects With Clinically Significant Changes From Baseline in Vital Signs[3]

End point description:

Vital signs (temperature, respiratory rate, pulse, systolic and diastolic blood pressure) were obtained with subjects in the seated position, after having sat/lied calmly for at least 5 minutes. Clinically significant vital signs criteria included Diastolic Blood Pressure (DBP) Value <50 mmHg, DBP Change ≥20 mmHg increase, DBP Change ≥20 mmHg decrease, Pulse Rate Value >120 beats per minute (bpm), Systolic Blood Pressure (SBP) Value <90 mmHg, SBP Change ≥30 mmHg increase, SBP Change ≥30mmHg decrease.
Overall number of subjects analyzed included all subjects who were randomized and received at least 1 confirmed dose of investigational product.

End point type	Primary

End point timeframe:

Baseline up to Day 29

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	259		
Units: Percentage of Subjects				
number (not applicable)				
Diastolic Blood Pressure (DBP) Value <50 mmHg	7.8	7.3		
DBP Change ≥20mmHg increase	2.3	3.5		
DBP Change ≥20mmHg decrease	3.9	3.1		
Pulse Rate Value >120 beats per minute (bpm)	2.3	1.9		
Systolic Blood Pressure (SBP) Value <90mmHg	23.3	26.3		
SBP Change ≥30mmHg increase	0	2.3		
SBP Change ≥30mmHg decrease	3.1	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Improvement in Investigator's Static Global Assessment (ISGA) at Day 29

End point title	Percentage of Subjects Achieving Improvement in Investigator's Static Global Assessment (ISGA) at Day 29

End point description:

ISGA assessed the severity of AD on a 5-point scale ranged from 0 (clear) to 4 (maximum severe), where higher scores indicate higher degree of AD. Grades for classification of severity: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe. Improvement in ISGA is defined as ISGA score of 0 or 1.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)	28.5 (20.4 to 36.6)	41.4 (35.4 to 47.5)		

Statistical analyses

Statistical analysis title	Crisaborole versus Vehicle
Comparison groups	Vehicle Twice a Day (BID) v Crisaborole 2% Twice a Day (BID)
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0124
Method	normal approximation to response rates
Parameter estimate	Risk difference (RD)
Point estimate	12.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	23.1

Secondary: Percentage of Subjects Achieving Success in ISGA at Day 29

End point title	Percentage of Subjects Achieving Success in ISGA at Day 29

End point description:

ISGA assessed the severity of AD on a 5-point scale ranged from 0 (clear) to 4 (maximum severe), where higher scores indicate higher degree of AD. Grades for classification of severity: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe. Success in ISGA is defined as an ISGA score of

Clear (0) or Almost Clear (1) with at least a 2 grade improvement from Baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary
End point timeframe:	
Baseline, Day 29	

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)	15.9 (9.4 to 22.5)	27.6 (22.1 to 33.1)		

Statistical analyses

Statistical analysis title	Crisaborole versus Vehicle
Comparison groups	Vehicle Twice a Day (BID) v Crisaborole 2% Twice a Day (BID)
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0078
Method	normal approximation to response rates
Parameter estimate	Risk difference (RD)
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	20.3

Secondary: Change From Baseline in Peak Pruritus Numeric Rating Scale (NRS) at Week 4-for Subjects ≥12 years

End point title	Change From Baseline in Peak Pruritus Numeric Rating Scale (NRS) at Week 4-for Subjects ≥12 years
End point description:	

Subject-rated pruritus score of lesions rated the severity of pruritus suffered in the past 24 hours on an 11-point NRS where 0 is no pruritus and 10 is worst itch imaginable. Change: score at Week 4 minus score at baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary
End point timeframe:	
Baseline, Week 4	

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	131		
Units: Units on a Scale				
least squares mean (confidence interval 95%)	-0.79 (-1.18 to -0.40)	-1.58 (-1.84 to -1.33)		

Statistical analyses

Statistical analysis title	Crisaborole versus Vehicle
Comparison groups	Vehicle Twice a Day (BID) v Crisaborole 2% Twice a Day (BID)
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	Mixed effect Model for Repeated Measures
Parameter estimate	LS mean of difference
Point estimate	-0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.33

Secondary: Percentage of Subjects Achieving Success in ISGA Over Time

End point title	Percentage of Subjects Achieving Success in ISGA Over Time

End point description:

ISGA assessed the severity of AD on a 5-point scale ranged from 0 (clear) to 4 (maximum severe), where higher scores indicate higher degree of AD. Grades for classification of severity: 0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, and 4 = severe.
Success in ISGA is defined as an ISGA score of Clear (0) or Almost Clear (1) with at least a 2 grade improvement from Baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 8	0.0 (-0.2 to 0.2)	4.8 (2.2 to 7.4)		
Day 15	4.9 (1.1 to 8.7)	11.6 (7.6 to 15.6)		
Day 22	10.8 (5.2 to 16.3)	18.1 (13.4 to 22.8)		
Day 29	15.9 (9.4 to 22.5)	27.6 (22.1 to 33.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Improvement in ISGA Over Time

End point title	Percentage of Subjects Achieving Improvement in ISGA Over Time

End point description:

ISGA assessed the severity of AD on a 5-point scale ranged from 0 (clear) to 4 (maximum severe), where higher scores indicate higher degree of AD.
Improvement in ISGA is defined as an ISGA score of Clear (0) or Almost Clear (1).
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 8	7.8 (3.2 to 12.4)	16.8 (12.3 to 21.4)		
Day 15	18.3 (11.6 to 25.1)	25.6 (20.2 to 31.0)		
Day 22	25.1 (17.4 to 32.7)	32.3 (26.6 to 38.1)		
Day 29	28.5 (20.4 to 36.6)	41.4 (35.4 to 47.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in EASI Total Score Over Time

End point title	Percent Change From Baseline in EASI Total Score Over Time

End point description:

The EASI quantifies the severity of a subject's AD based on both severity of lesion clinical signs and the percent of BSA affected. EASI is a composite scoring of the degree of erythema, induration/papulation, excoriation, and lichenification (each scored separately) for each of four 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. Total EASI score ranged from 0.0 to 72.0, higher scores = greater severity of AD.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	256		
Units: Percent Change				
least squares mean (confidence interval 95%)				
Day 8	-21.43 (-28.43 to -14.44)	-36.65 (-41.52 to -31.78)		
Day 15	-37.15 (-44.24 to -30.05)	-49.65 (-54.53 to -44.76)		
Day 22	-42.92 (-50.16 to -35.69)	-55.05 (-59.96 to -50.13)		
Day 29	-42.79 (-50.14 to -35.44)	-59.92 (-64.86 to -54.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Percent Body Surface Area (%BSA) Over Time

End point title	Change from Baseline in Percent Body Surface Area (%BSA) Over Time

End point description:

4 body regions were evaluated: head and neck, upper limbs, trunk (including axillae and groin) and lower limbs (including buttocks). Scalp was excluded. BSA was calculated using handprint method. Number of handprints (size of subject's hand with fingers in a closed position) fitting in the affected area of a body region was estimated.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	259		
Units: Percentage BSA				
least squares mean (confidence interval 95%)				
Day 8	-1.75 (-3.37 to -0.13)	-5.12 (-6.26 to -3.98)		
Day 15	-3.31 (-4.94 to -1.68)	-7.60 (-8.75 to -6.46)		
Day 22	-4.38 (-6.04 to -2.71)	-8.72 (-9.87 to -7.57)		
Day 29	-4.81 (-6.50 to -3.11)	-9.89 (-11.05 to -8.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving EASI-50 Over Time

End point title	Percentage of Subjects Achieving EASI-50 Over Time

End point description:

The EASI quantifies the severity of a subject's AD based on both severity of lesion clinical signs and the percent of BSA affected. The EASI score can vary in increments of range from 0.0 to 72.0, with higher scores representing greater severity of atopic dermatitis.
EASI-50 is defined as EASI score has ≥50% improvement from baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 8	18.5 (11.8 to 25.1)	37.1 (31.2 to 43.0)		
Day 15	32.7 (24.5 to 40.8)	58.9 (52.9 to 65.0)		
Day 22	42.2 (33.5 to 50.9)	66.4 (60.7 to 72.2)		

Day 29	49.4 (40.5 to 58.2)	72.7 (67.3 to 78.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving EASI-75 Over Time

End point title	Percentage of Subjects Achieving EASI-75 Over Time

End point description:

The EASI quantifies the severity of a subject's AD based on both severity of lesion clinical signs and the percent of BSA affected. The EASI score can vary in increments of range from 0.0 to 72.0, with higher scores representing greater severity of atopic dermatitis.
EASI-75 is defined as EASI score has ≥75% improvement from baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	260		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 8	6.1 (2.0 to 10.2)	11.2 (7.4 to 15.0)		
Day 15	15.4 (9.2 to 21.6)	26.3 (20.9 to 31.7)		
Day 22	26.3 (18.6 to 34.0)	38.2 (32.2 to 44.1)		
Day 29	27.6 (19.8 to 35.4)	46.4 (40.3 to 52.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Pruritus NRS Over Time-for Subjects ≥12 Years

End point title	Change From Baseline in Peak Pruritus NRS Over Time-for Subjects ≥12 Years

End point description:

Peak Pruritus NRS is subjects-rated pruritus score of lesions rated the severity of pruritus suffered in the past 24 hours on an 11-point NRS where 0 is no pruritus and 10 is worst itch imaginable.

Change: score at observation minus score at baseline.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 3, Week 4

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	131		
Units: Units on a Scale				
least squares mean (confidence interval 95%)				
Week 1	-0.38 (-0.75 to -0.01)	-0.94 (-1.19 to -0.69)		
Week 2	-0.53 (-0.90 to -0.15)	-1.26 (-1.52 to -1.01)		
Week 3	-0.64 (-1.02 to -0.26)	-1.41 (-1.66 to -1.16)		
Week 4	-0.79 (-1.18 to -0.40)	-1.58 (-1.84 to -1.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Reported Itch Severity Scale Over Time-for Subjects ≥6 Years and <12 Years

End point title	Change From Baseline in Patient Reported Itch Severity Scale Over Time-for Subjects ≥6 Years and <12 Years

End point description:

Patient Reported Itch Severity Scale is a 5-point scale indicating no itchy to very itchy (ranged from 0 to 4, where 0=no itch to 4=worst itch imaginable) for subjects ≥6 and <12 years of age.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 3, Week 4

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	76		
Units: Units on a Scale				
least squares mean (confidence interval 95%)				

	Week 1	-0.26 (-0.47 to -0.05)	-0.51 (-0.66 to -0.36)		
	Week 2	-0.22 (-0.43 to -0.01)	-0.70 (-0.85 to -0.55)		
	Week 3	-0.37 (-0.59 to -0.16)	-0.78 (-0.92 to -0.63)		
	Week 4	-0.52 (-0.74 to -0.30)	-0.86 (-1.00 to -0.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Observer Reported Itch Severity Scale Over Time-for Subjects <6 Years

End point title	Change From Baseline in Observer Reported Itch Severity Scale Over Time-for Subjects <6 Years

End point description:

Observer Reported Itch Severity Scale is an 11-point (ranged from 0 to 10, where 0=no itch to 10=worst itch imaginable) scale and must be completed by the observer (caregivers of subjects) for subjects <6 years of age.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 3, Week 4

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	41		
Units: Units on a Scale				
least squares mean (confidence interval 95%)				
Week 1	-0.31 (-0.80 to 0.17)	-1.03 (-1.44 to -0.62)		
Week 2	-0.73 (-1.22 to -0.24)	-1.68 (-2.10 to -1.27)		
Week 3	-0.96 (-1.46 to -0.47)	-1.79 (-2.21 to -1.38)		
Week 4	-1.25 (-1.75 to -0.75)	-1.95 (-2.37 to -1.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) Total

Score Over Time

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) Total Score Over Time

End point description:

The DLQI was a 10-item questionnaire that measures the impact of skin disease on subject's quality of life. The questionnaire will be completed by all subjects aged 16 years and older, based on the age at Screening Visit/time of informed consent/assent. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	117		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-1.1 (± 4.02)	-1.7 (± 3.57)		
Day 29	-1.5 (± 4.67)	-1.8 (± 4.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Dermatology Life Quality Index (CDLQI) Score Over Time

End point title	Change From Baseline in Children's Dermatology Life Quality Index (CDLQI) Score Over Time

End point description:

The CDLQI was a 10-item questionnaire that measures the impact of skin disease on children's (aged 4-15 years) quality of life. The CDLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	127		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-1.3 (± 5.18)	-3.6 (± 4.64)		
Day 29	-1.8 (± 6.00)	-3.9 (± 5.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Infants' Dermatitis Quality of Life Index (IDQOL) Total Score Over Time

End point title	Change From Infants' Dermatitis Quality of Life Index (IDQOL) Total Score Over Time

End point description:

The IDQOL was completed by observer for subjects aged 2-3 years, based on the age at the Screening Visit/time of informed consent/assent. The IDQOL is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score the more quality of life is impaired.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-1.3 (± 3.34)	-3.0 (± 3.30)		
Day 29	-0.7 (± 3.86)	-4.3 (± 4.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dermatitis Family Impact Questionnaire (DFI) Score Over Time

End point title	Change From Baseline in Dermatitis Family Impact Questionnaire (DFI) Score Over Time

End point description:

The DFI was completed by all observer for subjects aged 2-17 years, based on the age at Screening Visit/time of informed consent/assent. The minimum DFI score is 0; the maximum DFI score is 30. The higher score means worse outcome.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	148		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-0.5 (± 3.87)	-2.4 (± 4.66)		
Day 29	-2.1 (± 4.86)	-3.0 (± 5.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-Oriented Eczema Measure (POEM) Over Time in Subjects ≥12 Years

End point title	Change From Baseline in Patient-Oriented Eczema Measure (POEM) Over Time in Subjects ≥12 Years

End point description:

The POEM is a validated 7-item measure used to assess the impact of AD over the past week. The POEM contains 7 symptom based questions with responses rating number of days each symptom is experienced over the past week, from 0 (no days) to 4 (every day), with a maximum score of 28. Higher score means worse outcome.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	137		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-1.8 (± 5.25)	-5.4 (± 5.19)		
Day 29	-3.3 (± 5.38)	-5.7 (± 6.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in POEM Over Time in Subjects ≥2 Years and <12 Years

End point title	Change From Baseline in POEM Over Time in Subjects ≥2 Years and <12 Years

End point description:

The POEM is a validated 7-item measure used to assess the impact of AD over the past week. The POEM contains 7 symptom based questions with responses rating number of days each symptom is experienced over the past week, from 0 (no days) to 4 (every day), with a maximum score of 28. Higher score means worse outcome.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Day 15, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	123		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 15	-2.5 (± 5.17)	-6.7 (± 6.09)		
Day 29	-3.8 (± 5.33)	-7.7 (± 5.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Average of Patient Global Impression of Severity (PGIS) Score

End point title	Change From Baseline in Weekly Average of Patient Global Impression of Severity (PGIS) Score

End point description:

The PGIS (for subjects 12 years and older) is a single item patient-rated measure of the subject's AD condition severity at a given point in time.
This single item instrument uses a 7-point rating scale, which range from 1 to 7, where 1=Not present to 7=Extremely severe.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary
End point timeframe:	
Baseline, Week 1, Week 2, Week 3, Week 4	

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	133		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 1	-0.24 (± 0.511)	-0.43 (± 0.649)		
Week 2	-0.26 (± 0.692)	-0.60 (± 0.836)		
Week 3	-0.38 (± 0.871)	-0.66 (± 0.913)		
Week 4	-0.44 (± 0.965)	-0.71 (± 1.028)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) Score

End point title	Patient Global Impression of Change (PGIC) Score
End point description:	

The PGIC (for subjects 12 years and older) was used to determine global improvement as assessed by the patient. It was used as an anchor to define a responder definition for the peak pruritus scales for 'clinically important responder' and as a sensitivity analysis for defining a 'clinical important difference' on the peak pruritus scales.
This single item instrument is a 7-point rating scale, anchored by (1) 'very much improved' to (7) 'very much worse'.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary
End point timeframe:	
Day 8, Day 15, Day 22, Day 29	

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	137		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 8	3.3 (± 1.05)	2.6 (± 1.10)		
Day 15	3.2 (± 1.10)	2.6 (± 1.07)		

| | Day 22 | 3.0 (± 1.19) | 2.6 (± 1.04) | | |
| | Day 29 | 2.9 (± 1.21) | 2.5 (± 1.12) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Average of Observer Reported Global Impression of Severity (OGIS) Score

End point title	Change From Baseline in Weekly Average of Observer Reported Global Impression of Severity (OGIS) Score

End point description:

The OGIS (for subjects ≥2 and <12 years) is a single item observer-rated measure of the subject's AD condition severity at a given point in time.
This single item instrument uses a 7-point rating scale, which ranged from 1 to 7, where 1=Not present to 7=Extremely severe.
Overall number of subjects analyzed included all subjects randomized and dispensed study drug.
Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:

Baseline, Week 1, Week 2, Week 3, Week 4

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	119		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 1	-0.12 (± 0.593)	-0.62 (± 0.667)		
Week 2	-0.27 (± 0.617)	-0.93 (± 0.794)		
Week 3	-0.41 (± 0.770)	-1.03 (± 0.822)		
Week 4	-0.54 (± 0.854)	-1.14 (± 0.893)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observer Reported Global Impression of Change (OGIC) Score

End point title	Observer Reported Global Impression of Change (OGIC) Score

End point description:

The OGIC (for subjects ≥2 and <12 years) was used to determine global improvement as assessed by the observer. It was used as an anchor to define a responder definition for the peak pruritus scales for

'clinically important responder' and as a sensitivity analysis for defining a 'clinical important difference' on the peak pruritus scales.

This single item instrument is a 7-point rating scale, anchored by (1) 'very much improved' to (7) 'very much worse'.

Overall number of subjects analyzed included all subjects randomized and dispensed study drug. Subjects were assigned to the randomized treatment regardless of what treatment was received.

End point type	Secondary

End point timeframe:
Day 8, Day 15, Day 22, Day 29

End point values	Vehicle Twice a Day (BID)	Crisaborole 2% Twice a Day (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	123		
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Day 8	3.0 (± 1.08)	2.3 (± 0.81)		
Day 15	3.0 (± 1.10)	2.3 (± 0.92)		
Day 22	2.9 (± 1.16)	2.4 (± 0.99)		
Day 29	2.8 (± 1.07)	2.2 (± 1.05)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Baseline up to Day 60	
Adverse event reporting additional description:	
Same event may appear as AE and serious AE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety analysis set analyzed.	
Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Crisaborole 2% Twice a Day (BID)
Reporting group description:	
Crisaborole 2% was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	
Reporting group title	Vehicle Twice a Day (BID)
Reporting group description:	
Vehicle was applied BID for 28 days to the Treatable BSA identified at Baseline/Day 1 and new AD lesions that appear after the Baseline/Day 1.	

Serious adverse events	Crisaborole 2% Twice a Day (BID)	Vehicle Twice a Day (BID)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 260 (0.38%)	1 / 131 (0.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 260 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 260 (0.38%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Crisaborole 2% Twice a Day (BID)	Vehicle Twice a Day (BID)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 260 (38.85%)	43 / 131 (32.82%)	
General disorders and administration site conditions			
Application site discolouration			
subjects affected / exposed	9 / 260 (3.46%)	1 / 131 (0.76%)	
occurrences (all)	9	1	
Application site pain			
subjects affected / exposed	34 / 260 (13.08%)	5 / 131 (3.82%)	
occurrences (all)	41	6	
Application site paraesthesia			
subjects affected / exposed	7 / 260 (2.69%)	1 / 131 (0.76%)	
occurrences (all)	8	1	
Application site irritation			
subjects affected / exposed	3 / 260 (1.15%)	1 / 131 (0.76%)	
occurrences (all)	3	1	
Application site urticaria			
subjects affected / exposed	3 / 260 (1.15%)	0 / 131 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	6 / 260 (2.31%)	1 / 131 (0.76%)	
occurrences (all)	6	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 260 (1.15%)	0 / 131 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	4 / 260 (1.54%)	3 / 131 (2.29%)	
occurrences (all)	5	4	
Dermatitis atopic			
subjects affected / exposed	20 / 260 (7.69%)	15 / 131 (11.45%)	
occurrences (all)	22	15	
Pruritus			

subjects affected / exposed	0 / 260 (0.00%)	3 / 131 (2.29%)
occurrences (all)	0	3
Miliaria		
subjects affected / exposed	0 / 260 (0.00%)	2 / 131 (1.53%)
occurrences (all)	0	3
Dermatitis contact		
subjects affected / exposed	6 / 260 (2.31%)	1 / 131 (0.76%)
occurrences (all)	6	1
Urticaria		
subjects affected / exposed	3 / 260 (1.15%)	1 / 131 (0.76%)
occurrences (all)	3	1
Infections and infestations		
Conjunctivitis		
subjects affected / exposed	3 / 260 (1.15%)	2 / 131 (1.53%)
occurrences (all)	3	2
Folliculitis		
subjects affected / exposed	8 / 260 (3.08%)	6 / 131 (4.58%)
occurrences (all)	8	6
Gastroenteritis		
subjects affected / exposed	3 / 260 (1.15%)	0 / 131 (0.00%)
occurrences (all)	3	0
Nasopharyngitis		
subjects affected / exposed	9 / 260 (3.46%)	4 / 131 (3.05%)
occurrences (all)	9	6
Otitis media acute		
subjects affected / exposed	1 / 260 (0.38%)	2 / 131 (1.53%)
occurrences (all)	1	2
Upper respiratory tract infection		
subjects affected / exposed	9 / 260 (3.46%)	4 / 131 (3.05%)
occurrences (all)	10	4
Tonsillitis		
subjects affected / exposed	3 / 260 (1.15%)	0 / 131 (0.00%)
occurrences (all)	3	0
Pharyngitis		
subjects affected / exposed	3 / 260 (1.15%)	2 / 131 (1.53%)
occurrences (all)	3	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2019	Updated the primary and key secondary efficacy endpoints to align with global clinical development program, including: Change of primary endpoint from ISGA (Investigator's Static Global Assessment) to EASI (Eczema Area and Severity Index). Addition of ISGA as a key secondary endpoint. Addition of age specification for Pruritus assessments. Addition of tertiary endpoints pertaining to pruritus assessment.
28 August 2020	(1) Only for Japan: Japan subjects who completed the study intervention period in Study C3291032 were offered participation in the long-term safety extension study C3291027 if eligibility criteria were met. The subjects who rolled over into study C3291027 without a Post Treatment Follow Up period were considered completers in this study. (2) All female subjects who were of childbearing potential as applicable to the study who were, in the opinion of the investigator, sexually active and at risk for pregnancy with their partner(s) must have agreed to use an appropriate method of contraception consistently and correctly for the screening period, the duration of the active treatment period and for at least 28 days after the last dose of investigational product.
18 December 2020	Updated the sample size and power: The total sample size of 384 subjects in this study with a 2:1 randomization ratio (256:128) provided approximately 90% power to detect a 12% difference of percent change from baseline in EASI total score at Day 29 between crisaborole arm and vehicle arm at the 0.05 (2-sided) significance level, assuming the common standard deviation of percent change from baseline in EASI total score at Day 29 is 34%.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported