Clinical trial results:
A Phase 2B, Multi-Center, Randomized, Double-Blind, Vehicle Controlled, Intra-Subjects Study, to Evaluate Efficacy and Safety of two Regimens of Crisaborole Ointment 2% in Japanese Pediatric and Adult Subjects (2 Years and Older) With Mild to Moderate Atopic Dermatitis

Summary

EudraCT number	2020-000875-20
Trial protocol	Outside EU/EEA
Global end of trial date	16 December 2019

Results information

Result version number	v1 (current)
This version publication date	12 June 2020
First version publication date	12 June 2020

Trial information

Trial identification

Sponsor protocol code	C3291028

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03954158
WHO universal trial number (UTN)	-
Other trial identifiers	JapicCTI: JapicCTI-194776

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of crisaborole ointment 2%, administered QD or BID relative to the corresponding vehicle (QD or BID), on Total Sign Score (TSS) assessment in target lesions, in the treatment of mild to moderate AD in adults (cohort 1) and pediatrics (cohort 2).
To evaluate the efficacy of crisaborole ointment 2% BID relative to crisaborole ointment 2% QD, on TSS assessment in target lesions, in the treatment of mild to moderate AD in adults (cohort 1) and pediatrics (cohort 2).
To evaluate the efficacy of crisaborole ointment 2%, administered QD or BID, on TSS, ISGA and Pruritus assessments in target lesions, in the treatment of mild to moderate AD in adults (cohort 1) and pediatrics (cohort 2).
To assess the safety and local tolerability of crisaborole ointment 2%, administered QD or BID, in the treatment of mild to moderate AD in adults (cohort 1) and pediatrics (cohort 2)

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 Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 81
Worldwide total number of subjects	81
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)	40
Adolescents (12-17 years)	0
Adults (18-64 years)	41
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted for a total of 81 subjects between 15 June 2019 and 16 December 2019.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years

Arm description:

Subjects in this reporting arm were of age greater than or equal to (>=) 12 years. Investigator determined 2 target lesions of same atopic dermatitis (AD) severity in each subject at baseline (Day 1). Crisaborole ointment 2 percent (%) was applied once daily (QD) to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

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

Dosage and administration details:

Crisaborole ointment 2 % was applied QD to 1 of the target lesions.

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 QD to 1 of target lesions.

Arm title	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years

Arm description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied twice daily (BID) to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

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

Dosage and administration details:

Crisaborole ointment 2 % was applied BID to 1 of the target lesions.

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 1 of target lesions.

Arm title	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years

Arm description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Arm type	Experimental
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 QD to 1 of target lesions.

Investigational medicinal product name	Crisaborole 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Crisaborole ointment 2% was applied QD to 1 of the target lesions.

Arm title	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years

Arm description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

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

Dosage and administration details:

Crisaborole ointment 2% was applied BID to 1 of the target lesions.

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 1 of target lesions.

Number of subjects in period 1	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years
Started	20	21	20
Completed	20	21	20

Number of subjects in period 1	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age greater than or equal to (>=) 12 years. Investigator determined 2 target lesions of same atopic dermatitis (AD) severity in each subject at baseline (Day 1). Crisaborole ointment 2 percent (%) was applied once daily (QD) to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied twice daily (BID) to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group values	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years
Number of subjects	20	21	20
Age Categorical Units: Subjects			
<=18 years	1	0	20
Between 18 and 65 years	19	21	0
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	33.3	33.9	7.7
standard deviation	± 10.36	± 10.96	± 2.52
Sex: Female, Male Units: Subjects			
Female	11	17	8
Male	9	4	12
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	20	21	20
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	20	21	20
Unknown or Not Reported	0	0	0

Reporting group values	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years	Total	
Number of subjects	20	81	
Age Categorical			
Units: Subjects			
<=18 years	20	41	
Between 18 and 65 years	0	40	
>=65 years	0	0	
Age continuous			
Units: years			
arithmetic mean	7.8		
standard deviation	± 2.69	-	
Sex: Female, Male			
Units: Subjects			
Female	11	47	
Male	9	34	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	20	81	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	20	81	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age greater than or equal to (>=) 12 years. Investigator determined 2 target lesions of same atopic dermatitis (AD) severity in each subject at baseline (Day 1). Crisaborole ointment 2 percent (%) was applied once daily (QD) to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied twice daily (BID) to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% QD: Age group >=12 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle QD: Age group >=12 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Vehicle was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% BID: Age group >=12 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle BID: Age group >=12 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Vehicle was applied BID to 1 of the target lesions

for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% QD: Age group 2 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age 2 to 11. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle QD: Age group 2 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age 2 to 11. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Vehicle was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% BID: Age group 2 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age 2 to 11. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle BID: Age group 2 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this reporting arm were of age 2 to 11. Investigator determined 2 target lesions of same BID severity in each subject at baseline (Day 1). Vehicle was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% QD: All age group
Subject analysis set type	Full analysis

Subject analysis set description:

Crisaborole ointment 2% was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle QD: All age group
Subject analysis set type	Full analysis

Subject analysis set description:

Vehicle was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% BID: All age group
Subject analysis set type	Full analysis

Subject analysis set description:

Crisaborole ointment 2% was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle BID: All age group
Subject analysis set type	Full analysis

Subject analysis set description:

Vehicle was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this sub-group were of age 6 to 11 Years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle QD Sub-group: Age group 6 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this sub-group were of age 6 to 11 Years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Vehicle was applied QD to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this sub-group were of age 6 to 11 Years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Subject analysis set title	Vehicle BID Sub-group: Age group 6 to 11 years
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in this sub-group were of age 6 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Vehicle was applied BID to 1 of the target lesions for 15 days and subjects were followed up to 35 days after the end of treatment (maximum up to Day 50).

Primary: Change From Baseline in Total Sign Score (TSS) in Target Lesions at Day 15: Crisaborole Ointment 2% Versus Vehicle

End point title	Change From Baseline in Total Sign Score (TSS) in Target Lesions at Day 15: Crisaborole Ointment 2% Versus Vehicle

End point description:

Lesion TSS was an assessment of the target lesion severity, which was based on severity of 4 clinical signs erythema, induration/papulation, excoriation and lichenification. All of these 4 signs were rated on a scale of 0 to 3 (0= none, 1= mild, 2= moderate, 3= severe). These ratings were added to create a total TSS score; ranging from 0 (none) to 12 (most severe), with higher score representing greater severity. FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product.

End point type	Primary

End point timeframe:

Baseline, Day 15

End point values	Crisaborole 2% QD: Age group >=12 years	Vehicle QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Vehicle BID: Age group >=12 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	21	21
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	7.7 (± 0.36)	7.5 (± 0.45)	7.1 (± 0.46)	7.4 (± 0.48)
Change at Day 15	-4.5 (± 0.60)	-2.9 (± 0.51)	-4.8 (± 0.53)	-2.7 (± 0.47)

End point values	Crisaborole 2% QD: Age group 2 to 11 years	Vehicle QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years	Vehicle BID: Age group 2 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	6.2 (± 0.38)	6.5 (± 0.37)	7.1 (± 0.45)	7.3 (± 0.44)

Change at Day 15	-3.5 (± 0.47)	-2.0 (± 0.50)	-4.7 (± 0.50)	-2.6 (± 0.54)

Statistical analyses

Statistical analysis title	Crisaborole QD: >=12 yrs vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures (MMRM) included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0071
Method	Mixed models analysis
Parameter estimate	Least square mean of difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.53

Notes:

[1] - This was an intra-participant comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0029
Method	Mixed models analysis
Parameter estimate	Least square mean of difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[2] - This was an intra-participant comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.025
Method	Mixed models analysis
Parameter estimate	Least squares mean of difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[3] - This was an intra-participant comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0014
Method	Mixed models analysis
Parameter estimate	Least squares mean of difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[4] - This was an intra-participant comparison. Hence the actual number of subjects involved in the analysis was 20.

Secondary: Change From Baseline in Total Sign Score in Target Lesions at Day 15: Crisaborole Ointment 2% BID Versus Crisaborole Ointment 2% QD

End point title	Change From Baseline in Total Sign Score in Target Lesions at Day 15: Crisaborole Ointment 2% BID Versus Crisaborole Ointment 2% QD

End point description:

Lesion TSS was an assessment of the target lesion severity, which was based on severity of 4 clinical signs erythema, induration/papulation, excoriation and lichenification. All of these 4 signs were rated on a scale of 0 to 3 (0= none, 1= mild, 2= moderate, 3= severe). These ratings were added to create a total TSS score; ranging from 0 (none) to 12 (most severe), with higher score representing greater severity. FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline, Day 15

End point values	Crisaborole 2% QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Crisaborole 2% QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	21	20	20
Units: units on a scale				
least squares mean (confidence interval 95%)	-4.3 (-5.4 to -3.3)	-4.9 (-5.9 to -3.9)	-3.7 (-4.5 to -2.8)	-4.5 (-5.4 to -3.6)

Statistical analyses

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.4295

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.61

Secondary: Change From Baseline in Total Sign Score in Target Lesions at Day 8: Crisaborole Ointment 2% Versus Vehicle

End point title	Change From Baseline in Total Sign Score in Target Lesions at Day 8: Crisaborole Ointment 2% Versus Vehicle

End point description:

Lesion TSS was an assessment of the target lesion severity, which was based on severity of 4 clinical signs erythema, induration/papulation, excoriation and lichenification. All of these 4 signs were rated on a scale of 0 to 3 (0= none, 1= mild, 2= moderate, 3= severe). These ratings were added to create a total TSS score; ranging from 0 (none) to 12 (most severe), with higher score representing greater severity. FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product. Here, "n" signifies number of subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Day 8

End point values	Crisaborole 2% QD: Age group >=12 years	Vehicle QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Vehicle BID: Age group >=12 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	21	21
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (n= 20,20,21,21,20,20,20,20)	7.7 (± 0.36)	7.5 (± 0.45)	7.1 (± 0.46)	7.4 (± 0.48)
Change at Day 8 (n= 20,20,21,21,19,19,20,20)	-3.9 (± 0.49)	-2.0 (± 0.40)	-3.7 (± 0.53)	-2.3 (± 0.35)

End point values	Crisaborole 2% QD: Age group 2 to 11 years	Vehicle QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years	Vehicle BID: Age group 2 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: units on a scale				

arithmetic mean (standard error)				
Baseline (n= 20,20,21,21,20,20,20,20)	6.2 (± 0.38)	6.5 (± 0.37)	7.1 (± 0.45)	7.3 (± 0.44)
Change at Day 8 (n= 20,20,21,21,19,19,20,20)	-3.2 (± 0.34)	-1.9 (± 0.40)	-3.7 (± 0.46)	-2.0 (± 0.39)

Statistical analyses

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Least squares mean of difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.56

Notes:

[5] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Least squares mean of difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[6] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[7]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[7] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Least squares mean of difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.55

Notes:

[8] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.69

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.54

Secondary: Change from Baseline in Investigator's Static Global Assessment (ISGA) Score in Target Lesions at Day 8 and Day 15

End point title	Change from Baseline in Investigator's Static Global Assessment (ISGA) Score in Target Lesions at Day 8 and Day 15

End point description:

ISGA assessed the severity of AD on a 5-point scale ranged from 0 (clear) to 4 (severe), where higher scores indicated higher degree of AD. Grades for classification of severity: 0= clear (minor residual hypo/hyper pigmentation, no erythema or induration or papulation, no oozing or crusting), 1= almost clear (trace faint pink erythema, with barely perceptible induration or papulation and no oozing or crusting), 2= mild (faint pink erythema with mild induration or papulation and no oozing or crusting), 3= moderate (pink-red erythema with moderate induration or papulation with or without oozing or crusting) and 4= severe (deep or bright red erythema with severe induration or papulation and with oozing or crusting). FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product. Here, "n" signifies number of subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Day 8, Day 15

End point values	Crisaborole 2% QD: Age group >=12 years	Vehicle QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Vehicle BID: Age group >=12 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	21	21
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (n =20,20,21,21,20,20,20,20)	3.0 (± 0.0)	3.0 (± 0.0)	3.0 (± 0.0)	3.0 (± 0.0)
Change at Day 8 (n =20,20,21,21,19,19,20,20)	-1.3 (± 0.18)	-0.8 (± 0.12)	-1.1 (± 0.20)	-0.7 (± 0.12)
Change at Day 15 (n =20,20,21,21,20,20,20,20)	-1.9 (± 0.19)	-1.0 (± 0.15)	-1.9 (± 0.19)	-1.1 (± 0.19)

End point values	Crisaborole 2% QD: Age group 2 to 11 years	Vehicle QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years	Vehicle BID: Age group 2 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (n =20,20,21,21,20,20,20,20)	3.0 (± 0.0)	3.0 (± 0.0)	3.0 (± 0.0)	3.0 (± 0.0)
Change at Day 8 (n =20,20,21,21,19,19,20,20)	-1.4 (± 0.19)	-1.0 (± 0.20)	-1.2 (± 0.18)	-0.8 (± 0.16)
Change at Day 15 (n =20,20,21,21,20,20,20,20)	-1.8 (± 0.22)	-1.1 (± 0.19)	-1.9 (± 0.16)	-0.9 (± 0.20)

Statistical analyses

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs
Statistical analysis description:	
Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Least squares mean of difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.1

Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[9] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 8, Intra-suject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[10] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[11] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[12] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.27

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.26

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Least squares mean of difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[13] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[14]
Parameter estimate	Least squares mean of difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.25

Notes:

[14] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	Least squares mean of difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[15] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of visit, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[16]
Parameter estimate	Least squares mean of difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[16] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 15, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.27

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 15, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, visit, dosing regimen-by-visit interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.28

Secondary: Change From Baseline in Peak Pruritus Numerical Rating Scale (NRS) in Target Lesions up to Day 15 in Subjects Aged 12 Years or More

End point title	Change From Baseline in Peak Pruritus Numerical Rating Scale (NRS) in Target Lesions up to Day 15 in Subjects Aged 12 Years or More

End point description:

The severity of itch (pruritus) due to AD at the target lesion was assessed using the peak pruritus NRS. Subjects aged 12 years or more, were asked to rate their itch severity at the worst moment during the past 24 hours on a scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores represented more severe itch. FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15

End point values	Crisaborole 2% QD: Age group >=12 years	Vehicle QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Vehicle BID: Age group >=12 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	21	21
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	5.3 (± 0.59)	5.3 (± 0.57)	5.1 (± 0.47)	5.3 (± 0.43)
Change at Day 2	-1.3 (± 0.45)	-0.7 (± 0.38)	-0.6 (± 0.20)	-0.5 (± 0.37)
Change at Day 3	-1.7 (± 0.51)	-1.1 (± 0.49)	-1.4 (± 0.30)	-1.2 (± 0.36)
Change at Day 4	-2.5 (± 0.53)	-1.2 (± 0.55)	-2.0 (± 0.32)	-1.2 (± 0.44)
Change at Day 5	-2.6 (± 0.54)	-1.5 (± 0.46)	-2.6 (± 0.37)	-1.8 (± 0.40)
Change at Day 6	-2.8 (± 0.48)	-1.6 (± 0.51)	-2.2 (± 0.45)	-1.9 (± 0.46)
Change at Day 7	-2.9 (± 0.50)	-1.7 (± 0.56)	-2.5 (± 0.39)	-2.1 (± 0.45)
Change at Day 8	-3.2 (± 0.49)	-2.0 (± 0.56)	-2.8 (± 0.40)	-2.2 (± 0.48)
Change at Day 9	-3.2 (± 0.51)	-1.6 (± 0.55)	-2.7 (± 0.57)	-2.3 (± 0.46)
Change at Day 10	-3.3 (± 0.53)	-1.7 (± 0.61)	-3.0 (± 0.44)	-2.0 (± 0.58)
Change at Day 11	-3.5 (± 0.54)	-2.0 (± 0.55)	-3.1 (± 0.41)	-2.3 (± 0.49)
Change at Day 12	-3.5 (± 0.60)	-2.3 (± 0.58)	-3.3 (± 0.44)	-2.3 (± 0.50)
Change at Day 13	-3.4 (± 0.62)	-2.3 (± 0.57)	-3.5 (± 0.45)	-2.4 (± 0.46)
Change at Day 14	-3.3 (± 0.64)	-2.1 (± 0.65)	-3.6 (± 0.43)	-2.6 (± 0.47)
Change at Day 15	-3.5 (± 0.63)	-2.0 (± 0.63)	-3.7 (± 0.47)	-2.9 (± 0.46)

Statistical analyses

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 2, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[17] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 2, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[18]
Parameter estimate	Least squares mean of difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[18] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 2, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.54

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[19] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[20]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[20] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 3, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.55

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrss

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[21] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	Least squares mean of difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[22] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 4, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 5, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[23] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 5, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Least squares mean of difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[24] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 5, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.52

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[25] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[26]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:

[26] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 6, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.51

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 7, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[27] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 7, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[28]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[28] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 7, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.45

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[29]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[29] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[30]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.1

Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[30] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.44

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 9, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[31]
Parameter estimate	Least squares mean of difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[31] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 9, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[32]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[32] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 9, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	Least squares mean of difference
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[33] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[34] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 10, Inter-subject: Mixed effect Model for Repeated Measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of Least Squares Mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.49

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 11, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[35]
Parameter estimate	Least squares mean of difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[35] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 11, Intra-subject: MMRM included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[36]
Parameter estimate	Least squares mean of difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.38

Notes:

[36] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 11, Inter-subject: Mixed effect Model for Repeated Measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of Least Squares Mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.44

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[37]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[37] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[38]
Parameter estimate	Least squares mean of difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0

Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[38] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 12, Inter-subject: Mixed effect Model for Repeated Measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of Least Squares Mean
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.52

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 13, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[39]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[39] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 13, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[40]
Parameter estimate	Least squares mean of difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[40] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 13, Inter-subject: Mixed effect Model for Repeated Measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of Least Squares Mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.53

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[41]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[41] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[42]
Parameter estimate	Least squares mean of difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[42] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs

Statistical analysis description:

Change at Day 14, Inter-subject: Mixed effect Model for Repeated Measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value, and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of Least Squares Mean
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.53

Statistical analysis title	Crisaborole QD: >=12 yrs Vs Vehicle QD: >=12 yrs
Statistical analysis description:	
Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group >=12 years v Vehicle QD: Age group >=12 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[43]
Parameter estimate	Least squares mean of difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[43] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: >=12yrs Vs Vehicle BID: >=12yrs
Statistical analysis description:	
Change at Day 15, Intra-subject: Mixed effect model for repeated measures included the fixed effect of day, and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% BID: Age group >=12 years v Vehicle BID: Age group >=12 years
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other[44]
Parameter estimate	Least squares mean of difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[44] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 21.

Statistical analysis title	CrisaboroleQD:>=12 yrs Vs CrisaboroleBID:>=12 yrs
Statistical analysis description:	
Change at Day 15, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen, day, dosing regimen-by-day interaction, and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group >=12 years v Crisaborole 2% BID: Age group >=12 years

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least square mean
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.53

Secondary: Change From Baseline in Itch Severity Scale in Target Lesions up to Day 15 in Subjects Aged Between 6 to 11 Years

End point title	Change From Baseline in Itch Severity Scale in Target Lesions up to Day 15 in Subjects Aged Between 6 to 11 Years

End point description:

The itch severity scale was used for subjects >=6 to 11 years of age to assess severity of itch (pruritus) due to AD at the target lesion. In this assessment, subjects were asked to choose a unit that showed how itchy their skin had been on day of assessment on a 5-point scale ranging from 1= not itchy to 5= very itchy, where higher scores represented more severe itch. Analysis population included all subjects who were randomized and received greater than or equal to 1 dose of investigational product and aged between 6 to 11 years. Here, "Number of subjects Analyzed" signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Day 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15

End point values	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years	Vehicle QD Sub-group: Age group 6 to 11 years	Crisaborole 2% BID Sub-group: Age group 6 to 11 years	Vehicle BID Sub-group: Age group 6 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	16	14	14
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	1.6 (± 0.33)	1.8 (± 0.32)	1.9 (± 0.33)	1.6 (± 0.34)
Change at Day 2	-0.7 (± 0.36)	-0.33 (± 0.35)	-0.6 (± 0.45)	-0.4 (± 0.44)
Change at Day 3	-0.4 (± 0.35)	-0.5 (± 0.26)	-0.9 (± 0.30)	-0.3 (± 0.46)
Change at Day 4	-0.4 (± 0.45)	-0.4 (± 0.32)	-0.7 (± 0.46)	-0.7 (± 0.46)
Change at Day 5	-0.6 (± 0.41)	-0.1 (± 0.35)	-0.7 (± 0.47)	-0.3 (± 0.30)
Change at Day 6	-0.8 (± 0.37)	-0.4 (± 0.34)	-0.9 (± 0.38)	-0.8 (± 0.33)
Change at Day 7	-0.3 (± 0.46)	-0.3 (± 0.31)	-0.9 (± 0.45)	-0.8 (± 0.43)
Change at Day 8	-1.1 (± 0.30)	-0.7 (± 0.36)	-1.1 (± 0.44)	-0.6 (± 0.37)
Change at Day 9	-0.6 (± 0.38)	-0.3 (± 0.31)	-1.4 (± 0.37)	-1.0 (± 0.26)
Change at Day 10	-0.8 (± 0.37)	-0.4 (± 0.34)	-1.1 (± 0.33)	-0.9 (± 0.32)
Change at Day 11	-1.1 (± 0.34)	-0.5 (± 0.38)	-1.1 (± 0.49)	-0.7 (± 0.32)

Change at Day 12	-0.8 (± 0.32)	0.1 (± 0.40)	-1.4 (± 0.37)	-0.7 (± 0.45)
Change at Day 13	-0.8 (± 0.37)	-0.2 (± 0.34)	-1.4 (± 0.37)	-0.7 (± 0.44)
Change at Day 14	-0.9 (± 0.36)	-0.4 (± 0.31)	-1.3 (± 0.41)	-1.0 (± 0.36)
Change at Day 15	-0.8 (± 0.38)	-0.6 (± 0.26)	-1.3 (± 0.44)	-0.9 (± 0.38)

Statistical analyses

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 2, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[45]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:

[45] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 2, Intra-subjects: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[46]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[46] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 2, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.4

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[47]
Parameter estimate	Least squares mean of difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[47] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[48]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[48] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 3, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[49]
Parameter estimate	Least squares mean of difference
Point estimate	0

Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-1.1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[49] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[50]
Parameter estimate	Least squares mean of difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[50] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 4, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs
Statistical analysis description:	
Change at Day 5, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[51]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[51] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs
Statistical analysis description:	
Change at Day 5, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.	
Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[52]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[52] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs
Statistical analysis description:	
Change at Day 5, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.44

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[53]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[53] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[54]
Parameter estimate	Least squares mean of difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.7

Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[54] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 6, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 7, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[55]
Parameter estimate	Least squares mean of difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.43

Notes:

[55] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 7, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[56]
Parameter estimate	Least squares mean of difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[56] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 7, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.42

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[57]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[57] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[58]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[58] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.32

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs
Statistical analysis description:	
Change at Day 9, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[59]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[59] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs
Statistical analysis description:	
Change at Day 9, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.	
Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[60]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[60] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs
Statistical analysis description:	
Change at Day 9, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[61]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[61] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[62]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.6

Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[62] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 10, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.31

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 11, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[63]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[63] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 11, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure

UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.36

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 11, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[64]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[64] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[65]
Parameter estimate	Least squares mean of difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.43

Notes:

[65] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[66]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[66] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 12, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs
Statistical analysis description:	
Change at Day 13, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[67]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[67] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs
Statistical analysis description:	
Change at Day 13, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.	
Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[68]
Parameter estimate	Least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[68] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs
Statistical analysis description:	
Change at Day 13, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.34

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[69]
Parameter estimate	Least squares mean of difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[69] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[70]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.5

Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[70] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 14, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Crisaborole QD: 6-11yrs Vs Vehicle QD: 6-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Vehicle QD Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[71]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[71] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 16.

Statistical analysis title	Crisaborole BID: 6-11yrs Vs Vehicle BID: 6-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect model for repeated measures includes the fixed effect of day and the covariance structure AR1 is used.

Comparison groups	Crisaborole 2% BID Sub-group: Age group 6 to 11 years v Vehicle BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[72]
Parameter estimate	Least squares mean of difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.41

Notes:

[72] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 14.

Statistical analysis title	Crisaborole QD:6-11yrs Vs Crisaborole BID:6-11yrs

Statistical analysis description:

Change at Day 15, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD Sub-group: Age group 6 to 11 Years v Crisaborole 2% BID Sub-group: Age group 6 to 11 years
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.39

Secondary: Change From Baseline in Observer Reported Itch Severity Numerical Rating Scale in Target Lesions up to Day 15 in Subjects Aged Between 2 to 11 years

End point title	Change From Baseline in Observer Reported Itch Severity Numerical Rating Scale in Target Lesions up to Day 15 in Subjects Aged Between 2 to 11 years

End point description:

Observer reported itch severity NRS was used for subjects >=2 and < 12 years of age to assess severity of itch (pruritus) due to AD at the target lesion. Parents/caregivers (of subjects) were asked to rate subjects' itch (i.e. scratching, rubbing) at the worst moment during past 24 hours on a scale of 0 (no itch) to 10 (worst itch imaginable); higher scores represented more severe itch. FAS included all subjects who were randomized and received greater than or equal to 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Baseline, Day 15

End point values	Crisaborole 2% QD: Age group 2 to 11 years	Vehicle QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years	Vehicle BID: Age group 2 to 11 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: units on a scale				
arithmetic mean (standard error)				
Baseline	4.7 (± 0.56)	5.0 (± 0.50)	5.5 (± 0.56)	5.1 (± 0.56)
Change at Day 2	-0.5 (± 0.30)	-0.4 (± 0.31)	-0.7 (± 0.40)	-0.9 (± 0.50)
Change at Day 3	-0.7 (± 0.28)	-0.5 (± 0.35)	-1.6 (± 0.47)	-1.3 (± 0.55)
Change at Day 4	-0.5 (± 0.51)	-0.4 (± 0.38)	-1.8 (± 0.64)	-1.6 (± 0.58)
Change at Day 5	-1.4 (± 0.48)	-0.1 (± 0.60)	-2.0 (± 0.66)	-2.1 (± 0.52)
Change at Day 6	-1.9 (± 0.45)	-0.9 (± 0.43)	-2.7 (± 0.62)	-2.2 (± 0.66)
Change at Day 7	-2.0 (± 0.40)	-0.9 (± 0.45)	-3.0 (± 0.64)	-1.9 (± 0.71)
Change at Day 8	-2.3 (± 0.41)	-1.3 (± 0.36)	-3.3 (± 0.66)	-2.0 (± 0.70)
Change at Day 9	-2.0 (± 0.50)	-0.8 (± 0.42)	-3.4 (± 0.61)	-2.5 (± 0.63)
Change at Day 10	-2.2 (± 0.39)	-0.9 (± 0.42)	-3.9 (± 0.62)	-2.3 (± 0.65)
Change at Day 11	-2.4 (± 0.43)	-1.1 (± 0.45)	-3.5 (± 0.69)	-2.4 (± 0.66)
Change at Day 12	-2.1 (± 0.45)	-0.7 (± 0.61)	-4.1 (± 0.60)	-2.5 (± 0.65)
Change at Day 13	-2.1 (± 0.55)	-1.0 (± 0.50)	-4.1 (± 0.54)	-2.6 (± 0.70)
Change at Day 14	-2.4 (± 0.48)	-1.2 (± 0.49)	-4.3 (± 0.56)	-2.8 (± 0.66)
Change at Day 15	-2.5 (± 0.55)	-1.3 (± 0.45)	-4.3 (± 0.63)	-3.0 (± 0.61)

Statistical analyses

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 2, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[73]
Parameter estimate	Least squares mean of difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.39

Notes:

[73] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 2, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[74]
Parameter estimate	Least squares mean of difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.36

Notes:

[74] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 2, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.5

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[75]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[75] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 3, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[76]
Parameter estimate	Least squares mean of difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.58

Notes:

[76] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 3, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.53

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[77]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[77] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 4, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[78]
Parameter estimate	Least squares mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[78] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 4, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.74

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 5, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[79]
Parameter estimate	Least squares mean of difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.39

Notes:

[79] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 5, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[80]
Parameter estimate	Least squares mean of difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.66

Notes:

[80] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 5, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.7

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[81]
Parameter estimate	Least squares mean of difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.46

Notes:

[81] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 6, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[82]
Parameter estimate	Least squares mean of difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.47

Notes:

[82] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 6, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.63

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs
Statistical analysis description:	
Change at Day 7, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[83]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[83] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs
Statistical analysis description:	
Change at Day 7, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[84]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.48

Notes:

[84] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs
Statistical analysis description:	
Change at Day 7, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.61

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[85]
Parameter estimate	Least squares mean of difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[85] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 8, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[86]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.2

Variability estimate	Standard error of the mean
Dispersion value	0.52

Notes:

[86] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 8, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.64

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 9, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[87]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[87] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 9, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[88]
Parameter estimate	Least squares mean of difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[88] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 9, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.63

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[89]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[89] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 10, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[90]
Parameter estimate	Least squares mean of difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[90] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 10, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.58

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs
Statistical analysis description:	
Change at Day 11, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[91]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.54

Notes:

[91] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs
Statistical analysis description:	
Change at Day 11, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[92]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.51

Notes:

[92] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs
Statistical analysis description:	
Change at Day 11, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.	
Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.67

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[93]
Parameter estimate	Least squares mean of difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[93] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 12, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[94]
Parameter estimate	Least squares mean of difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.7

Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[94] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 12, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.63

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 13, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[95]
Parameter estimate	Least squares mean of difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[95] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 13, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[96]
Parameter estimate	Least squares mean of difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[96] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 13, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.62

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[97]
Parameter estimate	Least squares mean of difference
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[97] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 14, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 14, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[98]
Parameter estimate	Least squares mean of difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.62

Notes:

[98] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD: 2-11yrs Vs Vehicle QD: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Vehicle QD: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[99]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.57

Notes:

[99] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole BID: 2-11yrs Vs Vehicle BID: 2-11yrs

Statistical analysis description:

Change at Day 15, Intra-subject: Mixed effect Model for Repeated Measures included the fixed effect of day and the covariance structure UN was used.

Comparison groups	Crisaborole 2% BID: Age group 2 to 11 years v Vehicle BID: Age group 2 to 11 years
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[100]
Parameter estimate	Least squares mean of difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.46

Notes:

[100] - This was an intra-subject comparison. Hence the actual number of subjects involved in the analysis was 20.

Statistical analysis title	Crisaborole QD:2-11yrs Vs Crisaborole BID:2-11yrs

Statistical analysis description:

Change at Day 15, Inter-subject: Mixed effect model for repeated measures included the fixed effects of dosing regimen day dosing regimen-by-day interaction and baseline value and the covariance structure UN was used.

Comparison groups	Crisaborole 2% QD: Age group 2 to 11 years v Crisaborole 2% BID: Age group 2 to 11 years

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference of least squares mean
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.66

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) in the Target Lesions per Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) in the Target Lesions per Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term

End point description:

An AE was any untoward medical occurrence attributed to a subject who received study drug without regard to possibility of causal relationship. Treatment-emergent were events between first dose of study drug and up to end of study that were absent before treatment or that worsened relative to pre-treatment state. For this endpoint, treatment-emergent AEs occurred at each treated target lesion were summarized. MedDRA version 22.1 coding dictionary was used. Safety analysis set included all subjects receiving greater than or equal to 1 dose of investigational product. Treatment emergent AEs and SAEs occurred in target lesions were planned to be summarized by treatment in each regimen for each cohort and pooled cohort.

End point type	Secondary

End point timeframe:

Day 1 up to 35 days after end of treatment (maximum up to Day 50)

End point values	Crisaborole 2% QD: Age group >=12 years	Vehicle QD: Age group >=12 years	Crisaborole 2% BID: Age group >=12 years	Vehicle BID: Age group >=12 years
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	21	21
Units: subjects				
Application site coldness	0	0	0	1
Application site irritation	2	1	4	1
Application site pain	1	0	1	0
Application site pruritus	2	2	1	1
Application site folliculitis	1	0	1	0

End point values	Crisaborole 2% QD: Age group 2 to 11 years	Vehicle QD: Age group 2 to 11 years	Crisaborole 2% BID: Age group 2 to 11 years	Vehicle BID: Age group 2 to 11 years

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: subjects				
Application site coldness	0	0	0	0
Application site irritation	0	0	0	0
Application site pain	0	0	1	0
Application site pruritus	0	0	1	0
Application site folliculitis	0	0	0	0

End point values	Crisaborole 2% QD: All age group	Vehicle QD: All age group	Crisaborole 2% BID: All age group	Vehicle BID: All age group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	40	41	41
Units: subjects				
Application site coldness	0	0	0	1
Application site irritation	2	1	4	1
Application site pain	1	0	2	0
Application site pruritus	2	2	2	1
Application site folliculitis	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) And Serious Adverse Events (SAEs) by Treatment Regimen

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) And Serious Adverse Events (SAEs) by Treatment Regimen

End point description:

An AE was any untoward medical occurrence attributed to a subject who received study drug without regard to possibility of causal relationship. An 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. Treatment-emergent were events between first dose of study drug and up to end of study that were absent before treatment or that worsened relative to pre-treatment state. Safety analysis set included all subjects receiving greater than or equal to 1 dose of investigational product.

End point type	Secondary

End point timeframe:

Day 1 up to 35 days after end of treatment (maximum up to Day 50)

End point values	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	21	20	20
Units: subjects				
Subjects With AEs	6	6	2	2
Subjects With SAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to 35 days after end of treatment (maximum up to Day 50)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years

Reporting group description:

Subjects in this reporting arm were of age >=12 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subject were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each subject at baseline (Day 1). Crisaborole ointment 2% was applied QD to 1 of the target lesions and vehicle was applied QD to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Reporting group title	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years

Reporting group description:

Subjects in this reporting arm were of age 2 to 11 years. Investigator determined 2 target lesions of same AD severity in each Subjects at baseline (Day 1). Crisaborole ointment 2% was applied BID to 1 of the target lesions and vehicle was applied BID to another target lesion (intra-subject) for 15 days and subjects were followed up to maximum of 35 days after the end of treatment (maximum up to Day 50).

Serious adverse events	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11		

	years		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1: Crisaborole 2% QD + Vehicle QD, Age group >=12 years	Cohort 1:Crisaborole 2% BID + Vehicle BID,Age group >=12 years	Cohort 2:Crisaborole 2% QD + Vehicle QD, Age group 2-11 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)	6 / 21 (28.57%)	2 / 20 (10.00%)
General disorders and administration site conditions			
Application site coldness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Application site irritation			
subjects affected / exposed	3 / 20 (15.00%)	4 / 21 (19.05%)	0 / 20 (0.00%)
occurrences (all)	3	4	0
Application site pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Application site pruritus			
subjects affected / exposed	3 / 20 (15.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	3	2	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	3 / 21 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infections and infestations			
Application site folliculitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 2:Crisaborole 2% BID + Vehicle BID,Age group 2-11 years		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)		
General disorders and administration site conditions			
Application site coldness			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Application site irritation			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Application site pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Application site pruritus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue			

disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Infections and infestations Application site folliculitis subjects affected / exposed occurrences (all) Hand-foot-and-mouth disease subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0 1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported