Clinical trial results:
A Phase 3, Randomised, Double-Blind, Vehicle-Controlled Study to Evaluate the Efficacy and Safety of Maintenance Treatment and Flare Reduction With Crisaborole Ointment, 2%, Once Daily Over 52 Weeks in Pediatric and Adult Subjects (Ages 3 Months and Older) with Mild-to-Moderate Atopic Dermatitis, who Responded to Twice Daily Crisaborole Ointment, 2%, Treatment

Summary

EudraCT number	2019-000443-28
Trial protocol	AT ES FR
Global end of trial date	19 January 2022

Results information

Result version number	v1 (current)
This version publication date	16 July 2022
First version publication date	16 July 2022

Trial information

Trial identification

Sponsor protocol code	C3291035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04040192
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term efficacy of crisaborole ointment, 2%, once daily (QD) for maintenance therapy and flare reduction in paediatric and adult subjects >=3 months of age with mild-to-moderate atopic dermatitis (AD) who responded to crisaborole ointment, 2%, twice daily (BID) treatment.
To evaluate the safety and local tolerability of crisaborole ointment, 2%, QD for maintenance therapy and flare reduction in paediatric and adult subjects >=3 months of age with mild-to-moderate AD.

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 Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	China: 59
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	United States: 372
Worldwide total number of subjects	497
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)	20

Children (2-11 years)	202
Adolescents (12-17 years)	105
Adults (18-64 years)	155
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 620 subjects signed the informed consent form. 78 subjects were screen failures who did not meet eligibility criteria and were not enrolled. 542 subjects were enrolled, out of which only 497 were assigned to study treatment.

Period 1

Period 1 title	Open Label Period (up to 8 weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Crisaborole 2% BID

Arm description:

Subjects with mild to moderate AD were administered Crisaborole 2% ointment applied topically BID for maximum duration of up to 8 weeks in open label (OL) Run-in period.

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

Dosage and administration details:

2% (20 milligrams/gram) crisaborole ointment, applied topically twice daily.

Number of subjects in period 1	Crisaborole 2% BID
Started	497
Completed	270
Not completed	227
Physician decision	3
Consent withdrawn by subject	8
Failure to meet randomisation criteria	152
Adverse event	18
Unspecified	11
Lost to follow-up	14
Withdrawal by parent/guardian	18
Protocol deviation	3

Period 2

Period 2 title	Double blind Period (up to 52 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Vehicle QD

Arm description:

Subjects identified as responders during the OL period were randomised to receive vehicle applied topically QD for 52 weeks in the double-blind (DB) maintenance period. Subjects who developed flares during the DB maintenance period were switched to receive crisaborole 2% ointment BID in an open-label manner until resumption of DB treatment with vehicle.

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

Dosage and administration details:

Applied topically, once daily

Arm title	Crisaborole 2% QD

Arm description:

Subjects identified as responders during the OL period were randomised to receive Crisaborole 2% ointment applied topically QD for 52 weeks in the DB maintenance period. Subjects who developed flares during the DB maintenance period were switched to receive crisaborole 2% ointment BID in an open-label manner until resumption of DB treatment with crisaborole 2% QD.

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

Dosage and administration details:

2% (20 mg/g) crisaborole ointment, applied topically once daily

Number of subjects in period 2	Vehicle QD	Crisaborole 2% QD
Started	135	135
Completed	78	78
Not completed	57	57
Consent withdrawn by subject	6	11
Physician decision	-	2

Pregnancy	2	-
Adverse event	3	1
Unspecified	29	18
Lost to follow-up	6	10
Missing	2	5
Withdrawal by parent/guardian	8	7
Protocol deviation	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Crisaborole 2% BID
Reporting group description:	
Subjects with mild to moderate AD were administered Crisaborole 2% ointment applied topically BID for maximum duration of up to 8 weeks in open label (OL) Run-in period.	

Reporting group values	Crisaborole 2% BID	Total	
Number of subjects	497	497	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	20	20	
Children (2-11 years)	202	202	
Adolescents (12-17 years)	105	105	
Adults (18-64 years)	155	155	
From 65-84 years	15	15	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	19.89		
standard deviation	± 18.443	-	
Gender Categorical Units: Subjects			
Female	283	283	
Male	214	214	
Race Units: Subjects			
White	204	204	
Black or African American	161	161	
Asian	101	101	
American Indian or Alaska Native	2	2	
Native Hawaiian or Other Pacific Islander	1	1	
Multiracial	18	18	
Not reported	10	10	
Ethnicity Units: Subjects			
Hispanic or Latino	54	54	
Not Hispanic or Latino	426	426	
Not reported	17	17	

End points

End points reporting groups

Reporting group title	Crisaborole 2% BID
Reporting group description:	
Subjects with mild to moderate AD were administered Crisaborole 2% ointment applied topically BID for maximum duration of up to 8 weeks in open label (OL) Run-in period.	
Reporting group title	Vehicle QD
Reporting group description:	
Subjects identified as responders during the OL period were randomised to receive vehicle applied topically QD for 52 weeks in the double-blind (DB) maintenance period. Subjects who developed flares during the DB maintenance period were switched to receive crisaborole 2% ointment BID in an open-label manner until resumption of DB treatment with vehicle.	
Reporting group title	Crisaborole 2% QD
Reporting group description:	
Subjects identified as responders during the OL period were randomised to receive Crisaborole 2% ointment applied topically QD for 52 weeks in the DB maintenance period. Subjects who developed flares during the DB maintenance period were switched to receive crisaborole 2% ointment BID in an open-label manner until resumption of DB treatment with crisaborole 2% QD.	

Primary: Duration of Flare-Free Maintenance Until Onset of First-Flare During the Double Blind (DB) Period

End point title	Duration of Flare-Free Maintenance Until Onset of First-Flare During the Double Blind (DB) Period
End point description:	
The duration of flare-free maintenance is the time from randomization to the last Investigator's Static Global Assessment (ISGA) assessment and is right censored, if an intercurrent event (eg, death, dropout, loss to follow up, or end of study) occurs before the first flare. When a flare occurs first, the duration of flare free maintenance is the time from randomization to the first flare and is not censored. Duration of flare free maintenance was estimated using the Kaplan-Meier method. Evaluable-DB (Eval-DB) population included all randomised subjects with success in ISGA and Eczema Area Severity Index score (EASI50) criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period.	
End point type	Primary
End point timeframe:	
From randomisation to first flare or last ISGA assessment (up to 52 weeks)	

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Days				
median (confidence interval 95%)	30 (28 to 56)	111 (56 to 224)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0034 [1]
Method	Logrank

Notes:

[1] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)[2]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical study subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE was considered a TEAE if the event started on or after the treatment period start date and before end of study (at least 28 days after last dose of study intervention). Safety population comprised of all subjects who received at least 1 dose of study intervention during the study.

End point type	Primary

End point timeframe:

From start of study intervention up to 8 weeks (Crisaborole 2% BID arm); From start of study intervention in DB period up to 28 days after last dose of study intervention (maximum of 56 weeks) (for vehicle QD and crisaborole 2% QD)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a safety endpoint, and no statistical testing was conducted on any safety endpoints.

End point values	Crisaborole 2% BID	Vehicle QD	Crisaborole 2% QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	497	135	135	
Units: Subjects	109	49	36	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Flare-Free Days During the DB Period

End point title	Number of Flare-Free Days During the DB Period

End point description:

Flare - free days was the sum of the duration of flare-free maintenance of all QD periods during the maintenance period for each subject. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period.

End point type	Secondary

End point timeframe:

Up to maximum of 52 weeks

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Days				
least squares mean (standard error)	199.42 (± 11.824)	234.01 (± 12.323)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.0346
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	34.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.53
upper limit	66.64
Variability estimate	Standard error of the mean
Dispersion value	16.274

Notes:

[3] - Analysis of covariance (ANCOVA) model included fixed effects of treatment group, age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Number of Flares During the DB Period

End point title	Number of Flares During the DB Period

End point description:

Flare was defined as an ISGA score of >=2. The ISGA is a 5-point scale (0-4), reflecting a global assessment of AD severity based on erythema, induration/papulation, and oozing/crusting. ISGA score of 2: mild (faint pink erythema with mild induration/papulation and no oozing/crusting) 3: moderate (pink-red erythema with moderate induration/papulation with or without oozing/crusting) and 4: severe (deep or bright red erythema with severe induration/papulation and with oozing/crusting). Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period.

End point type	Secondary

End point timeframe:

Up to maximum of 52 weeks

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Flares				
median (full range (min-max))	1.00 (0.6 to 99999)	1.00 (0.4 to 99999)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.0042 [5]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0

Notes:

[4] - Median difference and 95%CI were estimated using Hodges-Lehmann method.

[5] - p-value was estimated by Wilcoxon rank sum test stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Duration of Pruritus Response Maintenance Until Onset of First Flare During the DB Period

End point title	Duration of Pruritus Response Maintenance Until Onset of First Flare During the DB Period

End point description:

Duration of maintenance of pruritus response was time from randomisation to loss of pruritus response or first flare onset (ISGA >=2) during 52-week DB period for subjects who were pruritus responders at randomisation. Pruritus(p) response maintenance was defined as maintenance of >=50% improvement in pruritus from baseline that was obtained at randomisation. If an event (e.g., death, first flare [ISGA >=2], lost to follow up, or end of study) occurred before loss of pruritus response for first flare-free period,duration of maintenance of pruritus response was time from randomisation to the last assessment and was censored. Eval-DB population was analysed. 99999: data not available. Here, 'number of subjects analysed (N): evaluable for this end point,'n': number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

From randomisation up to loss of pruritus response or onset of first flare or the last assessment (maximum of 52 weeks)

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	81		
Units: Days				
median (confidence interval 95%)				
≥12yrs:Baseline Peak p NRS≥3,≥3 pt reduced;n=25,37	99999 (18 to 99999)	164 (105 to 99999)		
≥12yrs:Baseline Peak p NRS≥4,≥4 pt reduced;n=18,24	99999 (16 to 99999)	309 (141 to 99999)		
6-<12yrs:Baseline PRIS Scale≥2,≥2pt reduced;n=10,2	99999 (2 to 99999)	133 (28 to 238)		
3mon-<6yrs:BaselineORISScale≥3,≥3pt reduce;n=20,10	7 (4 to 99999)	99999 (2 to 99999)		
3mon-<6yrs:BaselineORISScale≥4,≥4pt reduce;n=12,8	8 (4 to 99999)	99999 (2 to 99999)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1518 [6]
Method	Logrank

Notes:

[6] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6815 [7]
Method	Logrank

Notes:

[7] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3778 [8]
Method	Logrank

Notes:

[8] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.487 [9]
Method	Logrank

Notes:

[9] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1933 [10]
Method	Logrank

Notes:

[10] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Duration of Maintenance of Greater Than or Equal to (>=) 50% Reduction in Eczema Area and Severity Index (EASI) Total Score Until Onset of First Flare During the DB Period

End point title	Duration of Maintenance of Greater Than or Equal to (>=) 50% Reduction in Eczema Area and Severity Index (EASI) Total Score Until Onset of First Flare During the DB Period

End point description:

EASI:severity of AD based on severity of lesion clinical signs and%body surface area(BSA)affected.Severity of clinical signs of AD lesions(erythema (E),induration/papulation(I),excoriation(Ex),lichenification(L)):scored separately for each of 4 body regions(head and neck[h],upper limbs[u],trunk[t][including axillae and groin)],lower limbs[l][including buttocks])on4-point scale:0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA withAD:0 (0%),1(>0 to <10%),2(10 to <30%),3(30 to <50%),4(50 to <70%),5(70 to <90%),6(90 to 100%).Total score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score.For age<8 years old:Total score=0.2*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+ 0.3*Al*(El+Il+Exl+Ll).Total score:0.0to72.0,higher score:greater severity of AD.EASI response

End point type	Secondary

End point timeframe:

From randomisation to loss of EASI response or the last EASI assessment (up to maximum of 52 weeks)

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Days				
median (confidence interval 95%)	198 (84 to 99999)	99999 (175 to 99999)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1159 [11]
Method	Logrank

Notes:

[11] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Duration of Maintenance of Dermatology Life Quality Index (DLQI) Response Until Onset of First Flare During the DB Period

End point title	Duration of Maintenance of Dermatology Life Quality Index (DLQI) Response Until Onset of First Flare During the DB Period

End point description:

DLQI is a 10-item questionnaire that measured the impact of skin disease. Each question was evaluated on a 4-point scale (range 0 to 3) where, 0 = not at all, 1= a little, 2= a lot, 3= very much, where higher scores indicated more impact on quality of life. Scores from all 10 questions were added up to give DLQI total score, ranging from 0 (not at all) to 30 (very much). Higher scores indicated more impact on quality of life of subjects. DLQI response maintenance was defined as the response that does not lose more than minimal clinical important difference. 99999: data not available. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N' signifies subjects evaluable for this endpoint and 'n' signifies subjects evaluable at specific rows.

End point type	Secondary

End point timeframe:

From randomisation to loss of DLQI response or the last assessment up to first flare (up to maximum of 52 weeks)

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	82		
Units: Days				
median (confidence interval 95%)				
DLQI for subjects >=16 years of age (n=40, 41)	99999 (111 to 99999)	99999 (187 to 99999)		
Children's DLQI:subjects4-<16 yrs of age(n=46,41)	99999 (360 to 99999)	99999 (271 to 99999)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7456 [12]
Method	Logrank

Notes:

[12] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6973 [13]
Method	Logrank

Notes:

[13] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Duration of Maintenance of Patient Oriented Eczema Measure (POEM) Response Until Onset of First Flare During the DB Period

End point title	Duration of Maintenance of Patient Oriented Eczema Measure (POEM) Response Until Onset of First Flare During the DB Period

End point description:

POEM was a 7-item subject reported outcome measure used to assess the impact of AD (dryness, itching, flaking, cracking, sleep loss, bleeding and weeping) over the past week. Each item was scored as: no days=0, 1-2 days=1, 3-4 days=2, 5-6 days=3 and every day=4. The total score ranged from 0 to 28, where higher score indicated greater severity. POEM response maintenance was defined as the response that does not lose more than minimal clinical important difference. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. 99999: data not available. Here, 'N': subjects evaluable for this end point and 'number of subjects analysed': number of subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

From randomisation to loss POEM response or the last assessment up to the first flare (up to maximum of 52 weeks)

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	64		
Units: Days				
median (confidence interval 95%)				
POEM (n=31, 39)	55 (25 to 222)	180 (69 to 322)		
Proxy POEM (n=23, 25)	20 (13 to 124)	150 (33 to 99999)		

Statistical analyses

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0217 [14]
Method	Logrank

Notes:

[14] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Statistical analysis title	Crisaborole 2% QD vs Vehicle QD
Comparison groups	Vehicle QD v Crisaborole 2% QD
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0513 [15]
Method	Logrank

Notes:

[15] - p-value was estimated by the log-rank test, stratified by age group, duration of the BID treatment in OL period, and ISGA score at randomisation.

Secondary: Investigator's Static Global Assessment (ISGA) Score for the First Flare Period

End point title	Investigator's Static Global Assessment (ISGA) Score for the First Flare Period

End point description:

ISGA:5- point global assessment scale of AD severity, used to characterize overall disease severity across all treatable AD lesions (excluding the scalp). Score ranged from 0 to 4: where 0= clear(minor residual hypo/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting), 1= almost clear (trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting), 2= mild (faint pink erythema with mild induration/papulation and no oozing/crusting), 3= moderate (pink-red erythema with moderate induration/papulation with or without oozing/crusting), 4= severe (deep or bright red erythema with severe induration/papulation and with oozing/crusting). Higher scores: greater severity of AD. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and "n": number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Week 0 (Day 1), Week 4, Week 8 and Week 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	81		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=96, 81)	2.4 (± 0.51)	2.3 (± 0.47)		
Week 4 (n=53, 47)	2.2 (± 0.45)	2.2 (± 0.41)		
Week 8 (n=33,27)	2.1 (± 0.33)	2.4 (± 0.57)		
Week 12 (n=10, 11)	2.3 (± 0.48)	2.5 (± 0.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: EASI Score for the First Flare Period

End point title	EASI Score for the First Flare Period

End point description:

EASI:severity of subject's AD based on severity of lesion clinical signs and %BSA affected. Severity of clinical signs of AD lesions(erythema,induration/papulation, excoriation,lichenification)scored separately for each of 4 body regions(head and neck, upper limbs, trunk[including axillae and groin)],lower limbs[including buttocks])on 4-point scale: 0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA with AD in body region:0(0%), 1(>0 to <10%), 2(10to<30%), 3(30to<50%), 4(50to<70%), 5(70to<90%),6(90to100%).Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score; E=erythema;I =induration/papulation; Ex =excoriation; L=lichenification; h=head and neck; u=upper limbs;t=trunk;l= lower limbs.Total EASI score range:0.0 to 72.0,higher scores=greater severity of AD. Eval-DB population analysed. Here,'N':number of subjects evaluable for the end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Week 0 (Day 1), Week 4, Week 8 and Week 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	81		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=96, 81)	6.53 (± 5.897)	5.27 (± 3.933)		
Week 4 (n=54, 47)	6.09 (± 5.471)	5.02 (± 3.869)		
Week 8 (n=33, 27)	4.84 (± 5.322)	5.66 (± 4.459)		
Week 12 (n=10,11)	6.25 (± 4.546)	6.56 (± 5.647)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration (Days) of Flare Period

End point title	Duration (Days) of Flare Period

End point description:

Duration of flare period was average duration calculated from sum of durations/number of flares for each subject. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'Number of subjects analysed': number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	81		
Units: Days				
arithmetic mean (standard deviation)	54.2 (± 28.77)	55.3 (± 35.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in EASI Scores: OL Run-in Period

End point title	Percent Change From Baseline in EASI Scores: OL Run-in Period

End point description:

EASI:severity of subject's AD based on severity of lesion clinical signs and %BSA affected. Severity of clinical signs of AD lesions(erythema,induration/papulation, excoriation,lichenification)scored separately for each of 4 body regions(head and neck, upper limbs, trunk[including axillae and groin)],lower limbs[including buttocks])on 4-point scale: 0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA with AD in body region:0(0%), 1(>0 to <10%), 2(10to<30%), 3(30to<50%), 4(50to<70%), 5(70to<90%),6(90to100%).Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score; E=erythema;I =induration/papulation; Ex =excoriation; L=lichenification; h=head and neck; u=upper limbs;t=trunk;l= lower limbs.Total EASI score range:0.0 to 72.0,higher scores=greater severity of AD. Evaluable-OL (Eval-OL) population included all subjects that received at least 1 dose of study intervention in the OL period.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	497			
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at Week 2	-31.44 (± 37.151)			
Percent change at Week 4	-38.52 (± 44.448)			
Percent change at Week 6	-45.35 (± 49.453)			
Percent change at Week 8	-52.86 (± 51.209)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in EASI Scores: DB Period

End point title	Percent Change From Baseline in EASI Scores: DB Period

End point description:

EASI:severity of subject's AD based on severity of lesion clinical signs and %BSA affected. Severity of clinical signs of AD lesions(erythema,induration/papulation, excoriation,lichenification)scored separately for each of 4 body regions(head and neck, upper limbs, trunk[including axillae and groin)],lower limbs[including buttocks])on 4-point scale: 0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA with AD in body region:0(0%), 1(>0 to <10%), 2(10to<30%), 3(30to<50%), 4(50to<70%), 5(70to<90%),6(90to100%).Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score; E=erythema;I =induration/papulation; Ex =excoriation; L=lichenification; h=head and neck; u=upper limbs;t=trunk;l= lower limbs.Total EASI score range:0.0 to 72.0,higher scores=greater severity of AD. Eval-DB population analysed. Here,'N':number of subjects evaluable for the end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	57		
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at Week 4 (n=38, 57)	2.87 (± 72.981)	-10.16 (± 61.161)		
Percent change at Week 8 (n=42, 53)	1.04 (± 95.062)	34.26 (± 224.615)		
Percent change at Week 12 (n=44, 50)	-0.11 (± 126.465)	-8.22 (± 93.118)		
Percent change at Week 16 (n=53, 57)	26.30 (± 156.188)	27.98 (± 282.035)		

Percent change at Week 20 (n=8, 6)	26.38 (± 147.113)	-45.44 (± 54.768)		
Percent change at Week 24 (n=46, 50)	-20.62 (± 78.665)	6.94 (± 162.911)		
Percent change at Week 28 (n=9, 5)	19.17 (± 112.841)	-33.04 (± 31.617)		
Percent change at Week 32 (n=44, 45)	13.57 (± 131.633)	-19.33 (± 81.663)		
Percent change at Week 36 (n=3, 4)	-55.95 (± 51.052)	211.13 (± 155.547)		
Percent change at Week 40 (n=40, 40)	10.00 (± 142.168)	-12.94 (± 148.586)		
Percent change at Week 44 (n=10, 3)	-59.74 (± 34.119)	127.56 (± 322.953)		
Percent change at Week 48 (n=38, 39)	-22.23 (± 87.761)	-30.01 (± 72.497)		
Percent change at Week 52 (n= 42, 38)	-39.27 (± 72.619)	-49.81 (± 56.391)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in EASI Scores: First Flare Treatment Period

End point title	Percent Change From Baseline in EASI Scores: First Flare Treatment Period

End point description:

EASI:severity of subject’s AD based on severity of lesion clinical signs and %BSA affected. Severity of clinical signs of AD lesions(erythema,induration/papulation, excoriation,lichenification)scored separately for each of 4 body regions(head and neck, upper limbs, trunk[including axillae and groin)],lower limbs[including buttocks])on 4-point scale: 0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA with AD in body region:0(0%), 1(>0 to <10%), 2(10to<30%), 3(30to<50%), 4(50to<70%), 5(70to<90%),6(90to100%).Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score; E=erythema;I =induration/papulation; Ex =excoriation; L=lichenification; h=head and neck; u=upper limbs;t=trunk;l= lower limbs.Total EASI score range:0.0 to 72.0,higher scores=greater severity of AD. Eval-DB population analysed. Here,'N':number of subjects evaluable for the end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	57		
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at Week 0 (n=73, 57)	484.69 (± 672.923)	324.54 (± 484.380)		
Percent change at Week 4 (n=48, 35)	294.83 (± 350.182)	293.63 (± 461.044)		

Percent change at Week 8 (n=32, 22)	245.70 (± 411.541)	275.66 (± 447.181)		
Percent change at Week 12 (n=10, 11)	196.69 (± 272.911)	408.94 (± 665.204)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in EASI Scores: First Flare Free Period

End point title	Percent Change From Baseline in EASI Scores: First Flare Free Period

End point description:

EASI:severity of subject's AD based on severity of lesion clinical signs and %BSA affected. Severity of clinical signs of AD lesions(erythema,induration/papulation, excoriation,lichenification)scored separately for each of 4 body regions(head and neck, upper limbs, trunk[including axillae and groin)],lower limbs[including buttocks])on 4-point scale: 0=absent;1=mild;2=moderate;3=severe.EASI area score:%BSA with AD in body region:0(0%), 1(>0 to <10%), 2(10to<30%), 3(30to<50%), 4(50to<70%), 5(70to<90%),6(90to100%).Total EASI score =0.1*Ah*(Eh+Ih+Exh+Lh)+0.2*Au*(Eu+Iu+ExU+Lu)+0.3*At*(Et+It+Ext+Lt)+0.4*Al*(El+Il+Exl+Ll); A=EASI area score; E=erythema;I =induration/papulation; Ex =excoriation; L=lichenification; h=head and neck; u=upper limbs;t=trunk;l= lower limbs.Total EASI score range:0.0 to 72.0,higher scores=greater severity of AD. Eval-DB population analysed. Here,'N':number of subjects evaluable for the end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	56		
Units: Percent change				
arithmetic mean (standard deviation)				
Percent change at Week 4 (n=35, 56)	-0.46 (± 67.355)	-10.34 (± 61.699)		
Percent change at Week 8 (n=26, 48)	-21.34 (± 59.257)	10.36 (± 144.770)		
Percent change at Week 12 (n=24, 42)	2.24 (± 143.094)	-9.44 (± 100.314)		
Percent change at Week 16 (n=19, 37)	-14.82 (± 50.412)	-0.47 (± 109.386)		
Percent change at Week 20 (n=1, 4)	200.00 (± 99999)	-74.29 (± 40.808)		
Percent change at Week 24 (n=16, 32)	-35.57 (± 55.674)	-10.82 (± 109.364)		
Percent change at Week 28 (n=1, 2)	0.00 (± 99999)	-34.52 (± 48.824)		
Percent change at Week 32 (n=15, 26)	-28.39 (± 62.657)	-27.82 (± 94.806)		
Percent change at Week 36 (n=1, 0)	-67.86 (± 99999)	99999 (± 99999)		
Percent change at Week 40 (n=14, 22)	2.19 (± 83.621)	-47.60 (± 64.625)		

Percent change at Week 44 (n=1, 0)	-36.84 (± 99999)	99999 (± 99999)		
Percent change at Week 48 (n=14, 20)	-27.27 (± 61.689)	-39.13 (± 82.669)		
Percent change at Week 52 (n=12, 18)	-54.33 (± 45.072)	-59.87 (± 58.964)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ISGA Scores for OL run-in Period

End point title	Change From Baseline in ISGA Scores for OL run-in Period

End point description:

ISGA is a 5- point global assessment scale, used to characterize overall disease severity across all treatable AD lesions (excluding the scalp). Score ranged from 0 to 4: where 0= clear(minor residual hypo/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting), 1= almost clear (trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting), 2= mild (faint pink erythema with mild induration/papulation and no oozing/crusting), 3= moderate (pink-red erythema with moderate induration/papulation with or without oozing/crusting), 4= severe (deep or bright red erythema with severe induration/papulation and with oozing/crusting). Higher scores: greater severity of AD. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	497			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	2.7 (± 0.48)			
Change at Week 2	-0.5 (± 0.69)			
Change at Week 4	-0.7 (± 0.84)			
Change at Week 6	-0.9 (± 0.93)			
Change at Week 8	-1.2 (± 1.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ISGA Scores for DB Period

End point title	Change From Baseline in ISGA Scores for DB Period

End point description:

ISGA is a 5- point global assessment scale, used to characterize overall disease severity across all treatable AD lesions (excluding the scalp). Score ranged from 0 to 4: where 0= clear(minor residual

hypo/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting), 1= almost clear (trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting), 2= mild (faint pink erythema with mild induration/papulation and no oozing/crusting), 3= moderate (pink-red erythema with moderate induration/papulation with or without oozing/crusting), 4= severe (deep or bright red erythema with severe induration/papulation and with oozing/crusting). Higher scores: greater severity of AD. Eval-DB population was analysed. Here, 'n' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129, 125)	0.6 (± 0.50)	0.6 (± 0.49)		
Change at Week 4 (n=60, 81)	0.2 (± 0.52)	0.1 (± 0.49)		
Change at Week 8 (n=71, 80)	0.2 (± 0.50)	0.1 (± 0.58)		
Change at Week 12 (n=65, 76)	0.1 (± 0.52)	0.0 (± 0.54)		
Change at Week 16 (n=75, 83)	0.2 (± 0.46)	-0.0 (± 0.53)		
Change at Week 20 (n=13, 13)	0.3 (± 0.75)	0.2 (± 0.69)		
Change at Week 24 (n=70, 78)	0.0 (± 0.67)	-0.1 (± 0.56)		
Change at Week 28 (n=12, 6)	0.3 (± 0.45)	0.2 (± 0.41)		
Change at Week 32 (n=62, 72)	-0.0 (± 0.60)	-0.1 (± 0.53)		
Change at Week 36 (n=8, 5)	0.4 (± 0.74)	0.0 (± 0.00)		
Change at Week 40 (n=59, 64)	0.0 (± 0.57)	0.0 (± 0.59)		
Change at Week 44 (n=13, 8)	-0.1 (± 0.64)	0.3 (± 0.71)		
Change at Week 48 (n=58, 64)	0.1 (± 0.65)	-0.0 (± 0.63)		
Change at Week 52 (n=63, 63)	0.0 (± 0.66)	-0.0 (± 0.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ISGA Scores for First Flare Free Period

End point title	Change From Baseline in ISGA Scores for First Flare Free Period

End point description:

ISGA is a 5- point global assessment scale, used to characterize overall disease severity across all treatable AD lesions (excluding the scalp). Score ranged from 0 to 4: where 0= clear(minor residual hypo/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting), 1= almost clear (trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting), 2= mild (faint pink erythema with mild induration/papulation and no oozing/crusting), 3= moderate (pink-red erythema with moderate induration/papulation with or without oozing/crusting), 4= severe (deep or bright red erythema with severe induration/papulation and with oozing/crusting). Higher scores: greater severity of AD. Eval-DB population was analysed. 99999: data not available. Here, 'n' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129, 125)	0.6 (± 0.50)	0.6 (± 0.49)		
Change at Week 4 (n=55, 80)	0.2 (± 0.54)	0.1 (± 0.49)		
Change at Week 8 (n=43, 67)	0.2 (± 0.50)	0.1 (± 0.60)		
Change at Week 12 (n=37, 59)	0.1 (± 0.55)	-0.1 (± 0.54)		
Change at Week 16 (n=31, 52)	0.2 (± 0.43)	0.0 (± 0.52)		
Change at Week 20 (n=1, 5)	0.0 (± 99999)	-0.4 (± 0.55)		
Change at Week 24 (n=26, 46)	0.0 (± 0.63)	-0.1 (± 0.55)		
Change at Week 28 (n=2, 2)	0.5 (± 0.71)	0.0 (± 0.00)		
Change at Week 32 (n=25, 39)	-0.1 (± 0.64)	-0.1 (± 0.53)		
Change at Week 36 (n=1, 1)	0.0 (± 99999)	0.0 (± 99999)		
Change at Week 40 (n=23, 33)	0.0 (± 0.60)	-0.1 (± 0.66)		
Change at Week 44 (n=2, 3)	0.0 (± 0.00)	0.7 (± 0.58)		
Change at Week 48 (n=24, 32)	0.0 (± 0.66)	-0.1 (± 0.64)		
Change at Week 52 (n=22, 30)	0.0 (± 0.62)	-0.0 (± 0.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ISGA Scores for First Flare Treatment Period

End point title	Change From Baseline in ISGA Scores for First Flare Treatment Period

End point description:

ISGA:5-point global assessment scale, used to characterize overall disease severity across all treatable AD lesions (excluding scalp). Score ranged:0 to 4,where 0=clear(minor residual hypo/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting), 1=almost clear(trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting), 2=mild(faint pink erythema with mild induration/papulation and no oozing/crusting), 3=moderate(pink-red erythema with moderate induration/papulation with or without oozing/crusting), 4=severe(deep or bright red erythema with severe induration/papulation and with oozing/crusting). Higher scores:greater severity of AD. Flare treatment period:period between initiation of OL crisaborole2% ointment BID for treatment of flare developed during DB maintenance until resumption of DB treatment.Eval-DB population analysed. Here, 'N':subjects evaluable for this endpoint and 'n':subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	81		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=96, 81)	1.8 (± 0.57)	1.7 (± 0.49)		
Change at Week 4 (n=53, 47)	1.5 (± 0.54)	1.5 (± 0.55)		
Change at Week 8 (n=33, 27)	1.3 (± 0.47)	1.6 (± 0.74)		
Change at Week 12 (n=10, 11)	1.5 (± 0.53)	1.6 (± 0.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Treatable Percent Body Surface Area (% BSA): OL Run-in Period

End point title	Change from Baseline in Treatable Percent Body Surface Area (% BSA): OL Run-in Period

End point description:

The extent (%) to which a body region was involved with AD was determined using handprint method. Four body regions evaluated: head and neck (hn), upper limbs (ul), trunk (tr) (including axillae) and lower limbs (ll) (including buttocks). Total number of handprints=10 for hn, 20 for ul, 30 for tr, 40 for ll in subjects aged >=8 years; 20 for hn, 20 for ul, 30 for tr, 30 for ll in subjects aged 3 months to 7 years. Surface area of body region equivalent to 1 handprint: 10% for hn, 5% for ul, 3.33% for tr, 2.5% for ll in subjects aged >=8 years; 5% for hn, 5% for ul, 3.33% for tr, 3.33% for ll in subjects aged 3 months to 7 years. % BSA for a body region= total number of handprints in a body region * % surface area equivalent to 1 handprint. Overall % BSA for an individual=sum of % BSA across all 4 body regions and ranged from 0 to 100%, with higher values representing greater extent of BSA involvement with AD. Eval-OL population was analysed.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day) Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	497			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	19.61 (± 16.807)			
Change at Week 2	-3.86 (± 8.313)			
Change at Week 4	-5.09 (± 10.061)			

Change at Week 6	-6.42 (± 11.398)			
Change at Week 8	-7.35 (± 12.301)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Treatable %BSA: DB Period

End point title	Change from Baseline in Treatable %BSA: DB Period

End point description:

The extent (%) to which a body region was involved with AD was determined using handprint method. Four body regions evaluated: hn, ul, tr (including axillae) and ll (including buttocks). Total number of handprints=10 for hn, 20 for ul, 30 for tr, 40 for ll in subjects aged>=8 years; 20 for hn, 20 for ul, 30 for tr, 30 for ll in subjects aged 3 months to 7 years. Surface area of body region equivalent to 1 handprint: 10% for hn, 5% for ul, 3.33% for tr, 2.5% for ll in subjects aged >=8 years; 5% for hn, 5% for ul, 3.33% for tr, 3.33% for ll in subjects aged 3 months to 7 years. % BSA for a body region= total number of handprints in a body region * % surface area equivalent to 1 handprint. Overall % BSA for an individual=sum of %BSA across all 4 body regions and ranged from 0 to 100%,with higher values=greater extent of BSA involvement with AD. Eval-DB population was analysed. Here, 'n' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129, 125)	5.25 (± 9.588)	5.22 (± 7.170)		
Change at Week 4 (n=60, 81)	1.16 (± 4.391)	0.52 (± 5.164)		
Change at Week 8 (n=71, 80)	0.59 (± 6.202)	-0.19 (± 6.659)		
Change at Week 12 (n=65, 76)	1.20 (± 6.821)	0.26 (± 6.093)		
Change at Week 16 (n=75, 83)	1.25 (± 5.623)	0.58 (± 5.848)		
Change at Week 20 (n=13, 12)	-1.29 (± 5.363)	1.38 (± 6.846)		
Change at Week 24 (n=70, 78)	2.42 (± 9.213)	2.15 (± 11.217)		
Change at Week 28 (n=12, 6)	-0.30 (± 6.323)	-1.25 (± 5.906)		
Change at Week 32 (n=62, 72)	0.33 (± 7.623)	0.84 (± 5.971)		
Change at Week 36 (n=8, 5)	0.44 (± 1.917)	2.50 (± 3.623)		
Change at Week 40 (n=59, 64)	0.02 (± 6.752)	0.89 (± 6.097)		
Change at Week 44 (n=13, 7)	-2.56 (± 4.889)	0.57 (± 2.524)		
Change at Week 48 (=58, 64)	-0.37 (± 7.134)	0.48 (± 6.295)		

Change at Week 52 (n=63, 63)	-1.23 (± 5.531)	-1.91 (± 5.411)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Treatable %BSA: First Flare Free Period

End point title	Change from Baseline in Treatable %BSA: First Flare Free Period

End point description:

The extent (%) to which a body region was involved with AD was determined using handprint method. Four body regions evaluated: hn, ul, tr (including axillae) and ll (including buttocks). Total number of handprints=10 for hn, 20 for ul, 30 for tr, 40 for ll in subjects aged >=8 years; 20 for hn, 20 for ul, 30 for tr, 30 for ll in subjects aged 3 months to 7 years. Surface area of body region equivalent to 1 handprint: 10% for hn, 5% for ul, 3.33% for tr, 2.5% for ll in subjects aged >=8 years; 5% for hn, 5% for ul, 3.33% for tr, 3.33% for ll in subjects aged 3 months to 7 years. % BSA for a body region= total number of handprints in a body region * % surface area equivalent to 1 handprint. Overall % BSA for an individual=sum of % BSA across all 4 body regions and ranged from 0 to 100%, with higher values=greater extent of BSA involvement with AD. Eval-DB population was analysed. Here, 'n' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129, 125)	5.25 (± 9.588)	5.22 (± 7.170)		
Change at Week 4 (n=55, 80)	1.20 (± 4.487)	0.53 (± 5.196)		
Change at Week 8 (n=43, 67)	0.21 (± 7.661)	-0.10 (± 6.954)		
Change at Week 12 (n=37, 59)	0.96 (± 6.161)	0.05 (± 6.309)		
Change at Week 16 (n=31, 52)	1.05 (± 5.929)	0.28 (± 5.891)		
Change at Week 20 (n=1, 5)	5.00 (± 99999)	-0.60 (± 9.659)		
Change at Week 24 (n=26, 46)	2.46 (± 8.669)	3.09 (± 13.575)		
Change at Week 28 (n=2, 2)	-1.50 (± 2.121)	-3.00 (± 12.728)		
Change at Week 32 (n=25, 39)	0.40 (± 8.581)	0.91 (± 5.669)		
Change at Week 36 (n=1,1)	-2.00 (± 99999)	0.00 (± 99999)		
Change at Week 40 (n=23, 33)	-0.46 (± 7.881)	1.17 (± 6.153)		
Change at Week 44 (n=2, 3)	-3.25 (± 4.596)	2.33 (± 3.215)		

Change at Week 48 (n=24, 32)	-0.85 (± 7.724)	1.14 (± 6.959)		
Change at Week 52 (n=22, 30)	-1.50 (± 7.365)	-1.47 (± 5.232)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Treatable %BSA: First Flare Period

End point title	Change from Baseline in Treatable %BSA: First Flare Period

End point description:

The extent (%) to which a body region was involved with AD was determined using handprint method. Four body regions evaluated: hn, ul, tr (including axillae) and ll (including buttocks). Total number of handprints=10 for hn, 20 for ul, 30 for tr, 40 for ll in subjects aged >=8 years; 20 for hn, 20 for ul, 30 for tr, 30 for ll in subjects aged 3 months to 7 years. Surface area of body region equivalent to 1 handprint: 10% for hn, 5% for ul, 3.33% for tr, 2.5% for ll in subjects aged >=8 years; 5% for hn, 5% for ul, 3.33% for tr, 3.33% for ll in subjects aged 3 months to 7 years. % BSA for a body region= total number of handprints in a body region * % surface area equivalent to 1 handprint. Overall % BSA for an individual=sum of % BSA across all 4 body regions and ranged from 0 to 100%, with higher values=greater extent of BSA involvement with AD. Eval-DB population was analysed. Here, 'N':subjects evaluable for this endpoint and 'n':subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	81		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 0 (n=96, 81)	8.27 (± 12.154)	4.68 (± 6.304)		
Change at Week 4 (n=54, 47)	6.92 (± 9.704)	4.17 (± 6.884)		
Change at Week 8 (n=33, 27)	4.95 (± 11.642)	3.56 (± 6.646)		
Change at Week 12 (n=10, 11)	5.75 (± 10.499)	3.39 (± 5.328)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Most Commonly Affected Atopic Dermatitis (AD) % BSA: DB Period

End point title	Change from Baseline in Most Commonly Affected Atopic Dermatitis (AD) % BSA: DB Period

End point description:

The investigators were required to draw the skin areas affected by AD for each subject in a body map and the most commonly affected BSA was documented. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'n' signifies subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 24 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	125		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=129, 125)	14.28 (± 13.957)	10.77 (± 9.834)		
Change at Week 24 (n=72, 76)	2.29 (± 11.579)	-0.20 (± 3.919)		
Change at Week 52 (n=73, 75)	-3.46 (± 10.536)	-4.95 (± 7.731)		

Statistical analyses

No statistical analyses for this end point

Secondary: Night Time Itch Score: OL Run-in Period

End point title	Night Time Itch Score: OL Run-in Period

End point description:

The severity and frequency of itch (pruritus) during the night due to AD was assessed using a horizontal scale. Subjects 12 years of age or older were asked to assess their worst itching and frequency of itching due to AD during their most recent night's sleep on a scale. Score ranged from 0 to 10, 0(no itch) 10 (worst itch imaginable). Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	275			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Severity of night time itch: Baseline (n=248)	4.6 (± 3.02)			

Severity of night time itch: Week 2 (n=264)	2.9 (± 2.21)			
Severity of night time itch: Week 4 (n=266)	2.7 (± 2.25)			
Severity of night time itch: Week 6 (n=266)	2.5 (± 2.16)			
Severity of night time itch: Week 8 (n=266)	2.5 (± 2.19)			
Frequency of night time itch: Baseline (n=248)	4.4 (± 2.80)			
Frequency of night time itch: Week 2 (n=264)	2.8 (± 2.20)			
Frequency of night time itch: Week 4 (n=266)	2.7 (± 2.23)			
Frequency of night time itch: Week 6 (n=266)	2.4 (± 2.15)			
Frequency of night time itch: Week 8 (n=266)	2.4 (± 2.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Night Time Itch Score: DB Period

End point title	Night Time Itch Score: DB Period

End point description:

The severity and frequency of itch (pruritus) during the night due to AD was assessed using a horizontal scale. Subjects 12 years of age or older were asked to assess their worst itching and frequency of itching due to AD during their most recent night's sleep on a scale. Score ranged from 0 to 10, 0(no itch) 10 (worst itch imaginable). Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Severity of night time itch: Baseline (n=68, 76)	1.9 (± 1.71)	1.8 (± 1.79)		
Severity of night time itch: Week 4 (n=40, 58)	2.0 (± 1.83)	1.2 (± 1.49)		
Severity of night time itch: Week 8 (n=34, 52)	1.6 (± 1.61)	1.1 (± 1.59)		
Severity of night time itch: Week 12 (n=32, 52)	1.6 (± 1.74)	1.1 (± 1.64)		

Severity of night time itch: Week 16 (n=44, 51)	1.7 (± 1.85)	1.2 (± 1.70)		
Severity of night time itch: Week 20 (n=44, 49)	1.6 (± 1.86)	1.3 (± 1.86)		
Severity of night time itch: Week 24 (n=39, 48)	1.6 (± 1.71)	1.2 (± 1.79)		
Severity of night time itch: Week 28 (n=41, 48)	1.6 (± 1.69)	1.2 (± 1.73)		
Severity of night time itch: Week 32 (n=37, 46)	1.4 (± 1.57)	1.1 (± 1.74)		
Severity of night time itch: Week 36 (n=35, 46)	1.4 (± 1.56)	1.1 (± 1.85)		
Severity of night time itch: Week 40 (n=36, 45)	1.4 (± 1.46)	1.2 (± 1.95)		
Severity of night time itch: Week 44 (n=30, 45)	1.6 (± 1.69)	1.2 (± 1.98)		
Severity of night time itch: Week 48 (n=29, 43)	1.6 (± 1.76)	1.1 (± 1.93)		
Severity of night time itch: Week 52 (n=32, 40)	1.4 (± 1.69)	1.2 (± 1.96)		
Frequency of night time itch: Baseline (n=68, 76)	1.9 (± 1.66)	1.8 (± 1.79)		
Frequency of night time itch: Week 4 (n=40, 58)	1.9 (± 1.89)	1.1 (± 1.43)		
Frequency of night time itch: Week 8 (n=34, 52)	1.6 (± 1.71)	1.1 (± 1.55)		
Frequency of night time itch: Week 12 (n=32, 52)	1.5 (± 1.76)	1.1 (± 1.64)		
Frequency of night time itch: Week 16 (n=44, 51)	1.6 (± 1.87)	1.2 (± 1.64)		
Frequency of night time itch: Week 20 (44, 49)	1.6 (± 1.82)	1.3 (± 1.82)		
Frequency of night time itch: Week 24 (n= 39, 48)	1.5 (± 1.71)	1.2 (± 1.77)		
Frequency of night time itch: Week 28 (n=41, 48)	1.5 (± 1.71)	1.2 (± 1.70)		
Frequency of night time itch: Week 32 (n=37, 46)	1.3 (± 1.56)	1.0 (± 1.72)		
Frequency of night time itch: Week 36 (n=35, 46)	1.3 (± 1.57)	1.1 (± 1.82)		
Frequency of night time itch: Week 40 (n=36, 45)	1.4 (± 1.53)	1.2 (± 1.91)		
Frequency of night time itch: Week 44 (n=30, 45)	1.5 (± 1.71)	1.2 (± 1.95)		
Frequency of night time itch: Week 48 (n= 29, 43)	1.6 (± 1.78)	1.1 (± 1.87)		
Frequency of night time itch: Week 52 (n=32, 40)	1.3 (± 1.70)	1.2 (± 1.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Night Time Itch Score: First Flare Period

End point title	Night Time Itch Score: First Flare Period

End point description:

The severity and frequency of itch (pruritus) during the night due to AD was assessed using a horizontal

scale. Subjects 12 years of age or older were asked to assess their worst itching and frequency of itching due to AD during their most recent night's sleep on a scale. Score ranged from 0 to 10, 0(no itch) 10 (worst itch imaginable). Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Severity of night time itch: Week 0 (n=15, 17)	2.0 (± 1.12)	2.0 (± 2.32)		
Severity of night time itch: Week 4 (n=41, 39)	2.0 (± 1.95)	2.2 (± 2.18)		
Severity of night time itch: Week 8 (n=19, 15)	2.2 (± 1.73)	2.8 (± 2.60)		
Severity of night time itch: Week 12 (n=9, 16)	1.8 (± 1.32)	2.8 (± 2.03)		
Frequency of night time itch: Week 0 (n=15, 17)	2.0 (± 1.13)	2.0 (± 2.32)		
Frequency of night time itch: Week 4 (n=41, 39)	2.0 (± 2.13)	2.1 (± 2.11)		
Frequency of night time itch: Week 8 (n=19, 15)	2.1 (± 1.96)	2.6 (± 2.54)		
Frequency of night time itch: Week 12 (n=9, 16)	1.3 (± 1.26)	2.7 (± 2.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Night Time Itch Score: First Flare Free Period

End point title	Night Time Itch Score: First Flare Free Period

End point description:

The severity and frequency of itch (pruritus) during the night due to AD was assessed using a horizontal scale. Subjects 12 years of age or older were asked to assess their worst itching and frequency of itching due to AD during their most recent night's sleep on a scale. Score ranged from 0 to 10, 0(no itch) 10 (worst itch imaginable). Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Severity of night time itch: Baseline (n=68, 76)	1.9 (± 1.71)	1.8 (± 1.79)		
Severity of night time itch: Week 4 (n=38, 55)	2.0 (± 1.87)	1.2 (± 1.49)		
Severity of night time itch: Week 8 (n=27, 46)	1.8 (± 1.68)	1.2 (± 1.64)		
Severity of night time itch: Week 12 (n=22, 41)	1.5 (± 1.27)	1.1 (± 1.72)		
Severity of night time itch: Week 16 (n=19, 38)	1.7 (± 1.30)	1.2 (± 1.84)		
Severity of night time itch: Week 20 (n=18, 34)	1.6 (± 1.26)	1.4 (± 1.99)		
Severity of night time itch: Week 24 (n=18, 33)	1.6 (± 1.23)	1.2 (± 1.92)		
Severity of night time itch: Week 28 (n=17, 29)	1.6 (± 1.21)	1.2 (± 1.86)		
Severity of night time itch: Week 32 (n=17, 27)	1.5 (± 1.27)	1.2 (± 1.99)		
Severity of night time itch: Week 36 (n=17, 28)	1.5 (± 1.24)	1.1 (± 2.02)		
Severity of night time itch: Week 40 (n=17, 25)	1.6 (± 1.24)	1.1 (± 2.08)		
Severity of night time itch: Week 44 (n=16, 24)	1.9 (± 1.20)	1.1 (± 2.26)		
Severity of night time itch: Week 48 (n=16, 24)	1.5 (± 1.27)	1.2 (± 2.24)		
Severity of night time itch: Week 52 (n=12, 20)	1.6 (± 1.35)	1.2 (± 2.29)		
Frequency of night time itch: Baseline (n=68, 76)	1.9 (± 1.66)	1.8 (± 1.79)		
Frequency of night time itch: Week 4 (n=38, 55)	1.9 (± 1.93)	1.1 (± 1.43)		
Frequency of night time itch: Week 8 (n=27, 46)	1.8 (± 1.80)	1.1 (± 1.60)		
Frequency of night time itch: Week 12 (n=22, 41)	1.4 (± 1.31)	1.1 (± 1.73)		
Frequency of night time itch: Week 16 (n=19, 38)	1.6 (± 1.29)	1.2 (± 1.79)		
Frequency of night time itch: Week 20 (18, 34)	1.5 (± 1.16)	1.3 (± 1.92)		
Frequency of night time itch: Week 24 (n=18, 33)	1.4 (± 1.21)	1.2 (± 1.91)		
Frequency of night time itch: Week 28 (n=17, 29)	1.3 (± 1.19)	1.2 (± 1.89)		
Frequency of night time itch: Week 32 (n=17, 27)	1.3 (± 1.24)	1.1 (± 2.04)		
Frequency of night time itch: Week 36 (n=17, 28)	1.3 (± 1.22)	1.1 (± 2.05)		
Frequency of night time itch: Week 40 (n=17, 25)	1.6 (± 1.37)	1.1 (± 2.06)		

Frequency of night time itch: Week 44 (n=16, 24)	1.8 (± 1.22)	1.2 (± 2.25)		
Frequency of night time itch: Week 48 (n=16, 24)	1.5 (± 1.32)	1.3 (± 2.18)		
Frequency of night time itch: Week 52 (n=12, 20)	1.3 (± 1.38)	1.2 (± 2.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: AD Skin Pain Scores: OL Run-in Period

End point title	AD Skin Pain Scores: OL Run-in Period

End point description:

Subjects 12 years of age or older were asked to assess their worst skin pain due to AD at the analysis time, with the question: 'AD skin pain right now' using the skin pain numerical rating scale (NRS). Skin pain NRS was a 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	266			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=248)	2.6 (± 2.60)			
Week 2 (n=264)	2.0 (± 1.96)			
Week 4 (n=266)	1.9 (± 2.03)			
Week 6 (n=266)	1.8 (± 2.08)			
Week 8 (n=266)	1.7 (± 2.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: AD Skin Pain Scores: DB Period

End point title	AD Skin Pain Scores: DB Period

End point description:

Subjects 12 years of age or older were asked to assess their worst skin pain due to AD at the analysis time, with the question: 'AD skin pain right now' using the skin pain NRS. Skin pain NRS was a 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB

period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=68, 76)	1.1 (± 1.34)	1.2 (± 1.74)		
Week 4 (n=40, 58)	1.1 (± 1.55)	0.7 (± 1.27)		
Week 8 (n=34, 52)	1.0 (± 1.09)	1.0 (± 1.59)		
Week 12 (n=32, 52)	1.1 (± 1.69)	0.9 (± 1.62)		
Week 16 (n=44, 51)	1.3 (± 1.90)	1.1 (± 1.67)		
Week 20 (n=44, 49)	1.0 (± 1.49)	1.1 (± 1.81)		
Week 24 (n=39, 48)	1.1 (± 1.52)	1.0 (± 1.82)		
Week 28 (n=41, 48)	1.0 (± 1.54)	1.0 (± 1.78)		
Week 32 (n=37, 46)	1.0 (± 1.53)	0.8 (± 1.71)		
Week 36 (n=35, 46)	1.1 (± 1.61)	0.9 (± 1.78)		
Week 40 (n=36, 45)	1.1 (± 1.49)	1.1 (± 1.95)		
Week 44 (n=30, 45)	1.1 (± 1.67)	1.1 (± 1.99)		
Week 48 (n=29, 43)	1.3 (± 1.64)	0.9 (± 1.88)		
Week 52 (n=32, 40)	1.0 (± 1.62)	1.0 (± 1.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: AD Skin Pain Scores: First Flare Period

End point title	AD Skin Pain Scores: First Flare Period

End point description:

Subjects 12 years of age or older were asked to assess their worst skin pain due to AD at the analysis time, with the question: 'AD skin pain right now' using the skin pain NRS. Skin pain NRS was a 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8, 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=15, 17)	1.2 (± 1.26)	2.2 (± 2.01)		
Week 4 (n=41, 39)	1.4 (± 1.75)	1.7 (± 1.94)		
Week 8 (n=19, 15)	1.3 (± 1.53)	2.3 (± 2.15)		
Week 12 (n=9, 16)	2.0 (± 1.66)	2.3 (± 2.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: AD Skin Pain Scores: First Flare Free Period

End point title	AD Skin Pain Scores: First Flare Free Period

End point description:

Subjects 12 years of age or older were asked to assess their worst skin pain due to AD at the analysis time, with the question: 'AD skin pain right now' using the skin pain NRS. Skin pain NRS was a 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=68, 76)	1.1 (± 1.34)	1.2 (± 1.74)		
Week 4 (n=38, 55)	1.2 (± 1.58)	0.7 (± 1.30)		
Week 8 (n=27, 46)	1.0 (± 1.16)	1.0 (± 1.65)		
Week 12 (n=22, 41)	0.9 (± 1.17)	1.0 (± 1.75)		
Week 16 (n=19, 38)	1.1 (± 1.28)	1.1 (± 1.83)		
Week 20 (n=18, 34)	1.1 (± 1.18)	1.1 (± 2.02)		
Week 24 (n=18, 33)	1.2 (± 1.36)	1.0 (± 1.97)		
Week 28 (n=17, 29)	1.0 (± 1.35)	1.0 (± 2.04)		
Week 32 (n=17, 27)	1.1 (± 1.41)	1.0 (± 2.06)		
Week 36 (n=17, 28)	1.2 (± 1.44)	1.0 (± 2.08)		
Week 40 (n=17, 25)	1.2 (± 1.43)	1.1 (± 2.21)		
Week 44 (n=16, 24)	1.2 (± 1.48)	1.1 (± 2.37)		
Week 48 (n=16, 24)	1.3 (± 1.43)	1.0 (± 2.28)		

Week 52 (n=12, 20)	1.1 (± 1.46)	1.0 (± 2.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Severity Score: OL Run-in Period

End point title	Patient/Observer Global Impression of Severity Score: OL Run-in Period

End point description:

Patient/Observer Global Impression of Severity (PGIS/OGIS) is a single item subject or observer rated measure of the subject's AD condition severity at a given point in time using a 7-point rating scale, which ranges from 1 to 7, where 1=not present to 7=extremely severe. The PGIS was completed by all subjects ≥12 years of age and OGIS was completed by the observer for subjects 3 months-11 years of age. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	269			
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Baseline (n=247)	3.8 (± 1.30)			
>= 12 years of age: Week 2 (n=268)	3.2 (± 1.08)			
>= 12 years of age: Week 4 (n=269)	3.1 (± 1.12)			
>= 12 years of age: Week 6 (n=269)	3.0 (± 1.16)			
>= 12 years of age: Week 8 (n=269)	3.0 (± 1.19)			
3 months to <12 years of age: Baseline (n=207)	4.4 (± 1.20)			
3 months to <12 years of age: Week 2 (n=222)	3.3 (± 1.13)			
3 months to <12 years of age: Week 4 (n=222)	3.3 (± 1.15)			
3 months to <12 years of age: Week 6 (n=222)	3.2 (± 1.21)			
3 months to <12 years of age: Week 8 (n=222)	3.1 (± 1.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Severity Score: DB Period

End point title	Patient/Observer Global Impression of Severity Score: DB Period

End point description:

Patient/Observer Global Impression of Severity (PGIS/OGIS) is a single item subject or observer rated measure of the subject's AD condition severity at a given point in time using a 7-point rating scale, which ranges from 1 to 7, where 1=not present to 7=extremely severe. The PGIS was completed by all subjects ≥12 years of age and OGIS was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Baseline (n=68, 76)	2.6 (± 1.03)	2.5 (± 0.90)		
>= 12 years of age: Week 4 (n=40, 58)	2.7 (± 1.14)	2.3 (± 0.97)		
>= 12 years of age: Week 8 (n=34, 52)	2.6 (± 0.93)	2.2 (± 1.02)		
>= 12 years of age: Week 12 (n=32, 52)	2.7 (± 1.05)	2.2 (± 0.98)		
>= 12 years of age: Week 16 (n=44, 51)	2.7 (± 1.15)	2.3 (± 1.06)		
>= 12 years of age: Week 20 (n=44, 49)	2.7 (± 0.98)	2.4 (± 1.23)		
>= 12 years of age: Week 24 (n=39, 48)	2.6 (± 1.06)	2.4 (± 1.29)		
>= 12 years of age: Week 28 (n=41, 48)	2.7 (± 1.04)	2.4 (± 1.21)		
>= 12 years of age: Week 32 (n=37, 46)	2.6 (± 1.07)	2.4 (± 1.19)		
>= 12 years of age: Week 36 (n=35, 46)	2.7 (± 1.15)	2.4 (± 1.29)		
>= 12 years of age: Week 40 (n=36, 45)	2.6 (± 1.12)	2.4 (± 1.34)		
>= 12 years of age: Week 44 (n=30, 45)	2.6 (± 1.18)	2.5 (± 1.21)		
>= 12 years of age: Week 48 (n= 29, 43)	2.7 (± 1.27)	2.4 (± 1.19)		
>= 12 years of age: Week 52 (n=32, 40)	2.4 (± 1.19)	2.3 (± 1.26)		
3 months to <12 years of age: Baseline (n=58, 46)	2.6 (± 0.99)	2.6 (± 0.83)		
3 months to <12 years of age: Week 4 (n=26, 28)	2.6 (± 1.14)	2.4 (± 0.93)		

3 months to <12 years of age: Week 8 (n=29, 27)	2.3 (± 1.13)	2.4 (± 1.03)		
3 months to <12 years of age: Week 12 (n=32, 23)	2.3 (± 0.99)	2.2 (± 0.73)		
3 months to <12 years of age: Week 16 (n=32, 28)	2.4 (± 1.14)	2.1 (± 0.77)		
3 months to <12 years of age: Week 20 (n=31, 32)	2.4 (± 1.03)	2.2 (± 0.88)		
3 months to <12 years of age: Week 24 (n=32, 32)	2.4 (± 1.04)	2.3 (± 1.02)		
3 months to <12 years of age: Week 28 (n=31, 29)	2.4 (± 1.08)	2.0 (± 0.66)		
3 months to <12 years of age: Week 32 (n=27, 25)	2.1 (± 0.80)	2.1 (± 0.64)		
3 months to <12 years of age: Week 36 (n=25, 22)	2.4 (± 1.18)	2.0 (± 0.58)		
3 months to <12 years of age: Week 40 (n=25, 17)	2.2 (± 0.74)	2.1 (± 0.67)		
3 months to <12 years of age: Week 44 (n=26, 21)	2.3 (± 1.05)	2.0 (± 0.64)		
3 months to <12 years of age: Week 48 (n=26, 18)	2.2 (± 0.80)	1.8 (± 0.53)		
3 months to <12 years of age: Week 52 (n=26, 16)	2.1 (± 1.00)	1.7 (± 0.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Severity Score: First Flare Period

End point title	Patient/Observer Global Impression of Severity Score: First Flare Period

End point description:

PGIS/OGIS is a single item subject or observer rated measure of the subject's AD condition severity at a given point in time using a 7-point rating scale, which ranges from 1 to 7, where 1=not present to 7=extremely severe. The PGIS was completed by all subjects ≥12 years of age and OGIS was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	39		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Week 0 (n= 15, 17)	2.8 (± 0.93)	3.1 (± 1.10)		
>= 12 years of age: Week 4 (n=41, 39)	2.9 (± 0.98)	2.9 (± 1.14)		

>= 12 years of age: Week 8 (n=19, 15)	3.1 (± 1.02)	3.6 (± 1.17)		
>= 12 years of age: Week 12 (n=9, 16)	3.3 (± 1.56)	3.1 (± 1.50)		
3 months to <12 years of age: Week 0 (n=15, 11)	2.8 (± 0.94)	3.0 (± 0.79)		
3 months to <12 years of age: Week 4 (n=52, 36)	3.0 (± 1.19)	2.8 (± 0.90)		
3 months to <12 years of age: Week 8 (n=23, 17)	2.9 (± 1.16)	3.1 (± 1.03)		
3 months to <12 years of age: Week 12 (n=9, 6)	2.8 (± 0.95)	3.4 (± 0.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Severity Score: First Flare Free Period

End point title	Patient/Observer Global Impression of Severity Score: First Flare Free Period

End point description:

PGIS/OGIS is a single item subject or observer rated measure of the subject's AD condition severity at a given point in time using a 7-point rating scale, which ranges from 1 to 7, where 1=not present to 7=extremely severe. The PGIS was completed by all subjects ≥12 years of age and OGIS was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	76		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Baseline (n=68, 76)	2.6 (± 1.03)	2.5 (± 0.90)		
>= 12 years of age: Week 4 (n=40, 57)	2.7 (± 1.14)	2.3 (± 0.98)		
>= 12 years of age: Week 8 (n=29, 47)	2.6 (± 1.00)	2.3 (± 1.05)		
>= 12 years of age: Week 12 (n=22, 42)	2.6 (± 1.03)	2.2 (± 1.03)		
>= 12 years of age: Week 16 (n=20, 38)	2.6 (± 1.04)	2.1 (± 1.00)		
>= 12 years of age: Week 20 (n=18, 35)	2.7 (± 0.96)	2.2 (± 1.10)		
>= 12 years of age: Week 24 (n=18, 33)	2.7 (± 1.06)	2.2 (± 1.11)		
>= 12 years of age: Week 28 (n=17, 30)	2.7 (± 1.05)	2.2 (± 1.07)		

>= 12 years of age: Week 32 (n=17, 27)	2.6 (± 1.05)	2.1 (± 1.02)		
>= 12 years of age: Week 36 (n= 17, 28)	2.7 (± 1.05)	2.1 (± 1.08)		
>= 12 years of age: Week 40 (n=17, 25)	2.7 (± 1.10)	2.1 (± 1.10)		
>= 12 years of age: Week 44 (n=16, 24)	2.7 (± 1.10)	2.3 (± 1.24)		
>= 12 years of age: Week 48 (n=16, 24)	2.6 (± 1.14)	2.3 (± 1.28)		
>= 12 years of age: Week 52 (n=14, 21)	2.6 (± 1.15)	2.0 (± 1.25)		
3 months to <12 years of age: Baseline (n=58, 46)	2.6 (± 0.99)	2.6 (± 0.83)		
3 months to <12 years of age: Week 4 (n=26, 28)	2.6 (± 1.14)	2.4 (± 0.93)		
3 months to <12 years of age: Week 8 (n=19, 22)	2.5 (± 1.28)	2.3 (± 0.98)		
3 months to <12 years of age: Week 12 (n=18, 17)	2.3 (± 1.12)	2.3 (± 0.78)		
3 months to <12 years of age: Week 16 (n=16, 16)	2.4 (± 1.14)	2.0 (± 0.84)		
3 months to <12 years of age: Week 20 (n=11, 15)	2.3 (± 1.24)	2.1 (± 0.83)		
3 months to <12 years of age: Week 24 (n=10, 14)	2.3 (± 1.47)	1.9 (± 0.59)		
3 months to <12 years of age: Week 28 (n=9, 13)	2.4 (± 1.59)	2.0 (± 0.57)		
3 months to <12 years of age: Week 32 (n=8, 13)	1.8 (± 0.75)	2.1 (± 0.58)		
3 months to <12 years of age: Week 36 (n=8, 9)	2.6 (± 1.77)	1.7 (± 0.56)		
3 months to <12 years of age: Week 40 (n=8, 7)	2.0 (± 0.99)	1.8 (± 0.60)		
3 months to <12 years of age: Week 44 (n=8, 9)	2.7 (± 1.66)	1.7 (± 0.56)		
3 months to <12 years of age: Week 48 (n=7,7)	2.1 (± 0.92)	1.7 (± 0.41)		
3 months to <12 years of age: Week 52 (n=7, 6)	1.5 (± 0.50)	1.6 (± 0.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Change Score: OL Run-in Period

End point title	Patient/Observer Global Impression of Change Score: OL Run-in Period

End point description:

Patient/Observer Global Impression of Change (PGIC/OGIC) is a single item instrument using 7-point rating scale and was used to determine global improvement at a given point in time since the start of study drug. The scores ranged from 1=very much improved to 7=very much worse. The PGIC was completed by all subjects ≥12 years of age and OGIC was completed by the observer for subjects 3 months-11 years of age. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	273			
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Week 2 (n=271)	2.8 (± 1.17)			
>= 12 years of age: Week 4 (n=273)	2.7 (± 1.32)			
>= 12 years of age: Week 6 (n=273)	2.6 (± 1.36)			
>= 12 years of age: Week 8 (n=273)	2.6 (± 1.46)			
3 months to <12 years: Week 2 (n=222)	2.6 (± 1.21)			
3 months to <12 years: Week 4 (n=222)	2.6 (± 1.36)			
3 months to <12 years: Week 6 (n=222)	2.5 (± 1.50)			
3 months to <12 years: Week 8 (n=222)	2.5 (± 1.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Change Score: DB Period

End point title	Patient/Observer Global Impression of Change Score: DB Period

End point description:

PGIC/OGIC is a single item instrument using 7-point rating scale and was used to determine global improvement at a given point in time since the start of study drug. The scores ranged from 1=very much improved to 7=very much worse. The PGIC was completed by all subjects ≥12 years of age and OGIC was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Baseline (n=69, 78)	1.8 (± 0.68)	1.8 (± 0.75)		
>= 12 years of age: Week 4 (n=32, 51)	1.9 (± 0.84)	1.8 (± 0.76)		
>= 12 years of age: Week 8 (n=36, 50)	2.0 (± 0.74)	1.9 (± 0.88)		
>= 12 years of age: Week 12 (n=32, 49)	2.0 (± 0.76)	1.9 (± 1.00)		
>= 12 years of age: Week 16 (n=42, 52)	2.1 (± 1.00)	1.8 (± 0.79)		
>= 12 years of age: Week 20 (n=21, 21)	2.3 (± 1.10)	1.6 (± 0.80)		
>= 12 years of age: Week 24 (n=37, 47)	1.7 (± 0.70)	1.8 (± 1.10)		
>= 12 years of age: Week 28 (n=18, 17)	2.2 (± 1.06)	1.6 (± 0.80)		
>= 12 years of age: Week 32 (n=34, 45)	1.7 (± 0.72)	1.8 (± 1.26)		
>= 12 years of age: Week 36 (n=17, 17)	1.9 (± 0.93)	1.8 (± 0.66)		
>= 12 years of age: Week 40 (n=34, 47)	1.8 (± 0.91)	1.8 (± 1.10)		
>= 12 years of age: Week 44	1.8 (± 0.79)	1.8 (± 0.75)		
>= 12 years of age: Week 48 (n=30, 43)	1.5 (± 0.63)	1.9 (± 1.34)		
>= 12 years of age: Week 52 (n=32, 43)	1.8 (± 0.76)	1.6 (± 1.01)		
3 months to <12 years of age: Baseline (n=60, 47)	1.5 (± 0.60)	1.6 (± 0.61)		
3 months to <12 years of age: Week 4 (n=24, 24)	1.7 (± 0.95)	2.0 (± 1.23)		
3 months to <12 years of age: Week 8 (n=30, 24)	1.5 (± 0.57)	1.8 (± 0.98)		
3 months to <12 years of age: Week 12 (n=29, 26)	1.6 (± 0.68)	1.5 (± 0.65)		
3 months to <12 years of age: Week 16 (n=26, 28)	1.8 (± 0.97)	1.5 (± 0.58)		
3 months to <12 years of age: Week 20 (n=16, 17)	1.9 (± 0.72)	1.4 (± 0.62)		
3 months to <12 years of age: Week 24 (n=27, 29)	1.7 (± 0.90)	1.7 (± 0.77)		
3 months to <12 years of age: Week 28 (n=16, 19)	1.6 (± 0.73)	1.4 (± 0.68)		
3 months to <12 years of age: Week 32 (n=25, 24)	1.9 (± 1.24)	1.8 (± 1.09)		
3 months to <12 years of age: Week 36 (n=13, 15)	1.6 (± 0.51)	1.5 (± 0.64)		
3 months to <12 years of age: Week 40 (n= 21, 16)	1.9 (± 0.85)	1.7 (± 0.87)		
3 months to <12 years of age: Week 44 (n=13, 12)	1.6 (± 0.51)	1.8 (± 1.14)		
3 months to <12 years of age: Week 48 (n=22, 20)	1.6 (± 0.67)	1.6 (± 0.89)		
3 months to <12 years of age: Week 52 (n= 29, 20)	1.6 (± 0.78)	1.5 (± 0.60)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Change Score: First Flare Period

End point title	Patient/Observer Global Impression of Change Score: First Flare Period

End point description:

PGIC/OGIC is a single item instrument using 7-point rating scale and was used to determine global improvement at a given point in time since the start of study drug. The scores ranged from 1=very much improved to 7=very much worse. The PGIC was completed by all subjects ≥12 years of age and OGIC was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	44		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Week 0 (n=43, 44)	3.8 (± 1.56)	3.1 (± 1.51)		
>= 12 years of age: Week 4 (n=21, 24)	2.7 (± 1.42)	2.9 (± 1.30)		
>= 12 years of age: Week 8 (n=13, 15)	2.4 (± 0.51)	3.2 (± 1.26)		
>= 12 years of age: Week 12 (n=3, 7)	2.7 (± 0.58)	3.7 (± 1.11)		
3 months to <12 years of age: Week 0 (n=46, 33)	3.8 (± 1.84)	3.3 (± 1.53)		
3 months to <12 years of age: Week 4 (n=28, 21)	2.4 (± 0.95)	2.6 (± 0.97)		
3 months to <12 years of age: Week 8 (n=18, 11)	2.3 (± 0.97)	3.0 (± 1.41)		
3 months to <12 years of age: Week 12 (n=5, 2)	2.4 (± 0.55)	4.5 (± 0.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient/Observer Global Impression of Change Score: First Flare Free

Period	
End point title	Patient/Observer Global Impression of Change Score: First Flare Free Period

End point description:

PGIC/OGIC is a single item instrument using 7-point rating scale and was used to determine global improvement at a given point in time since the start of study drug. The scores ranged from 1=very much improved to 7=very much worse. The PGIC was completed by all subjects ≥12 years of age and OGIC was completed by the observer for subjects 3 months-11 years of age. Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not reported.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
>= 12 years of age: Baseline (n=69, 78)	1.8 (± 0.68)	1.8 (± 0.75)		
>= 12 years of age: Week 4 (n=30, 51)	2.0 (± 0.83)	1.8 (± 0.76)		
>= 12 years of age: Week 8 (n=25, 44)	2.1 (± 0.73)	1.9 (± 0.90)		
>= 12 years of age: Week 12 (n=20, 40)	2.0 (± 0.86)	2.0 (± 1.04)		
>= 12 years of age: Week 16 (n=19, 37)	2.3 (± 1.29)	1.8 (± 0.76)		
>= 12 years of age: Week 20 (n=8, 13)	1.9 (± 0.64)	1.5 (± 0.52)		
>= 12 years of age: Week 24 (n=17, 31)	1.8 (± 0.83)	1.6 (± 0.80)		
>= 12 years of age: Week 28 (n=7, 9)	1.9 (± 0.69)	1.4 (± 0.53)		
>= 12 years of age: Week 32 (n=16, 27)	1.7 (± 0.60)	1.6 (± 0.97)		
>= 12 years of age: Week 36 (n=6,7)	2.0 (± 1.26)	1.4 (± 0.53)		
>= 12 years of age: Week 40 (n=17, 26)	1.7 (± 0.85)	1.5 (± 0.58)		
>= 12 years of age: Week 44 (n=7, 9)	2.1 (± 1.07)	1.6 (± 0.73)		
>= 12 years of age: Week 48 (n=17, 24)	1.5 (± 0.62)	1.6 (± 1.10)		
>= 12 years of age: Week 52 (n=15, 23)	1.7 (± 0.88)	1.4 (± 0.50)		
3 months to <12 years of age: Baseline (n=60, 47)	1.5 (± 0.60)	1.6 (± 0.61)		
3 months to <12 years of age: Week 4 (n=22, 24)	1.8 (± 0.97)	2.0 (± 1.23)		
3 months to <12 years of age: Week 8 (n=15, 18)	1.7 (± 0.62)	1.8 (± 1.00)		
3 months to <12 years of age: Week 12 (n=15, 18)	1.7 (± 0.80)	1.6 (± 0.62)		
3 months to <12 years of age: Week 16 (n=10, 14)	1.6 (± 0.97)	1.6 (± 0.63)		

3 months to <12 years of age: Week 20 (n=3, 9)	1.7 (± 0.58)	1.4 (± 0.73)		
3 months to <12 years of age: Week 24 (n=7, 14)	1.6 (± 0.53)	1.6 (± 0.84)		
3 months to <12 years of age: Week 28 (n=3, 9)	1.0 (± 0.00)	1.3 (± 0.71)		
3 months to <12 years of age: Week 32 (n=8, 11)	1.6 (± 0.52)	1.7 (± 0.90)		
3 months to <12 years of age: Week 36 (n=1, 8)	1.0 (± 99999)	1.5 (± 0.53)		
3 months to <12 years of age: Week 40 (n=7, 8)	1.7 (± 0.76)	1.3 (± 0.46)		
3 months to <12 years of age: Week 44 (n=1, 5)	1.0 (± 99999)	1.4 (± 0.55)		
3 months to <12 years of age: Week 48 (n=6, 7)	1.5 (± 0.55)	1.3 (± 0.49)		
3 months to <12 years of age: Week 52 (n=7, 7)	1.1 (± 0.38)	1.3 (± 0.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Outcomes Study Sleep Scale Score: OL Run-in Period

End point title	Medical Outcomes Study Sleep Scale Score: OL Run-in Period

End point description:

The Medical Outcomes Study (MOS) Sleep Scale is a 12-item measure that is segregated into subscales addressing seven sleep domains (i.e. sleep disturbance, snoring, short of breath(B) or headache(H), adequacy of sleep, somnolence, sleep problems index I and sleep problems index II). An additional single item assessed quantity of sleep. The sleep domains and problems index I and problems index II were scored on a range of 0-100, and higher scores indicated worse outcomes. The quantity of sleep scores ranged from 0 to 24 (number of hours slept). The optimal sleep sub-scale score is a binary outcome derived from Sleep Quantity (SQ): the response is Yes (or 1) if SQ= 7 or 8 hours per night. Observed scores for each individual sleep domain and quantity of sleep are reported in this end point. Eval-OL population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	273			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Quantity Hours Slept Score: Baseline (n=268)	7.4 (± 3.27)			
Quantity Hours Slept Score: Week 2 (n=271)	7.6 (± 3.06)			
Quantity Hours Slept Score: Week 4 (n=273)	7.6 (± 3.24)			

Quantity Hours Slept Score: Week 6 (n=273)	7.9 (± 3.43)			
Quantity Hours Slept Score: Week 8 (n=273)	7.8 (± 3.41)			
Optimal Hours Slept Score: Baseline (n=268)	0.4 (± 0.50)			
Optimal Hours Slept Score: Week 2 (n=271)	0.5 (± 0.50)			
Optimal Hours Slept Score: Week 4 (n=273)	0.5 (± 0.50)			
Optimal Hours Slept Score: Week 6 (n=273)	0.5 (± 0.50)			
Optimal Hours Slept Score: Week 8 (n=273)	0.5 (± 0.50)			
Short of B or H score: Baseline(n=268)	27.8 (± 15.18)			
Short of B or H score: Week 2 (n=271)	27.6 (± 13.98)			
Short of B or H score: Week 4 (n=273)	27.0 (± 14.56)			
Short of B or H score: Week 6 (n=273)	27.0 (± 13.95)			
Short of B or H score: Week 8 (n=273)	26.4 (± 14.00)			
Snoring Score: Baseline (n=268)	43.3 (± 27.34)			
Snoring Score: Week 2 (n=271)	41.1 (± 26.73)			
Snoring Score: Week 4 (n=273)	41.0 (± 26.02)			
Snoring Score: Week 6 (n=273)	40.9 (± 26.44)			
Snoring Score: Week 8 (n=273)	40.5 (± 26.09)			
Sleep Disturbance Score: Baseline (n=268)	45.0 (± 21.27)			
Sleep Disturbance Score: Week 2 (n= 271)	40.0 (± 20.21)			
Sleep Disturbance Score: Week 4 (n=273)	40.3 (± 21.20)			
Sleep Disturbance Score: Week 6 (n=273)	38.5 (± 20.25)			
Sleep Disturbance Score: Week 8 (n=273)	38.6 (± 20.93)			
Sleep Adequacy Score: Baseline (n=268)	63.0 (± 19.99)			
Sleep Adequacy Score: Week 2 (n=271)	66.1 (± 20.64)			
Sleep Adequacy Score: Week 4 (n=273)	65.5 (± 20.67)			
Sleep Adequacy Score: Week 6 (n=273)	66.8 (± 20.12)			
Sleep Adequacy Score: Week 8 (n=273)	67.3 (± 20.33)			
Sleep Somnolence Score: Baseline (n=268)	44.9 (± 18.01)			
Sleep Somnolence Score: Week 2 (n=271)	42.5 (± 17.19)			
Sleep Somnolence Score: Week 4 (n=273)	42.5 (± 18.12)			
Sleep Somnolence Score: Week 6 (n=273)	42.5 (± 17.93)			
Sleep Somnolence Score: Week 8 (n=273)	42.5 (± 19.08)			
Sleep Problems Index I Score: Baseline (n=268)	38.3 (± 14.74)			
Sleep Problems Index I Score: Week 2 (n=271)	35.3 (± 13.83)			
Sleep Problems Index I Score: Week 4 (n=273)	36.1 (± 14.97)			
Sleep Problems Index I Score: Week 6 (n=273)	34.9 (± 14.08)			

Sleep Problems Index I Score: Week 8 (n=273)	34.7 (± 14.03)			
Sleep Problems Index II Score: Baseline (n=268)	41.5 (± 15.39)			
Sleep Problems Index II Score: Week 2 (n=271)	37.7 (± 14.67)			
Sleep Problems Index II Score: Week 4 (n=273)	38.1 (± 15.73)			
Sleep Problems Index II Score: Week 6 (n=273)	36.9 (± 14.82)			
Sleep Problems Index II Score: Week 8 (n=273)	36.6 (± 15.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Outcomes Study Sleep Scale Score: DB Period

End point title	Medical Outcomes Study Sleep Scale Score: DB Period

End point description:

The MOS Sleep Scale is a 12-item measure that is segregated into subscales addressing seven sleep domains (i.e. sleep disturbance, snoring, short of breath or headache, adequacy of sleep, somnolence, sleep problems index I and sleep problems index II). An additional single item assessed quantity of sleep. The sleep domains and problems index I and problems index II were scored on a range of 0-100, and higher scores indicated worse outcomes. The quantity of sleep scores ranged from 0 to 24 (number of hours slept). The optimal sleep sub-scale score is a binary outcome derived from SQ: the response is Yes (or 1) if SQ= 7 or 8 hours per night. Observed scores for each individual sleep domain and quantity of sleep are reported in this end point. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period),Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Quantity Hours Slept Score: Baseline (n=69, 78)	8.3 (± 3.79)	7.5 (± 2.42)		
Quantity Hours Slept Score: Week 4 (n=31, 51)	8.9 (± 4.55)	8.1 (± 3.32)		
Quantity Hours Slept Score: Week 8 (n=36, 50)	8.1 (± 3.31)	7.8 (± 3.72)		
Quantity Hours Slept Score: Week 12 (n=32, 49)	8.8 (± 4.46)	7.5 (± 3.18)		
Quantity Hours Slept Score: Week 16 (n=42, 52)	8.2 (± 3.89)	8.1 (± 4.35)		
Quantity Hours Slept Score: Week 20 (n=21, 21)	6.9 (± 1.28)	7.3 (± 1.49)		

Quantity Hours Slept Score: Week 24 (n=37, 47)	8.0 (± 4.21)	8.0 (± 4.33)		
Quantity Hours Slept Score: Week 28 (n=18, 17)	8.4 (± 5.20)	7.2 (± 1.38)		
Quantity Hours Slept Score: Week 32 (n=34, 45)	9.2 (± 5.64)	8.3 (± 3.70)		
Quantity Hours Slept Score: Week 36 (n=17, 17)	6.9 (± 1.58)	7.2 (± 1.48)		
Quantity Hours Slept Score: Week 40 (n=34, 47)	8.1 (± 4.39)	8.1 (± 3.92)		
Quantity Hours Slept Score: Week 44 (n=18, 17)	7.1 (± 2.04)	6.7 (± 0.99)		
Quantity Hours Slept Score: Week 48 (n=30, 43)	7.6 (± 3.88)	7.7 (± 3.06)		
Quantity Hours Slept Score: Week 52 (n=32, 43)	7.7 (± 4.30)	7.7 (± 3.12)		
Optimal Hours Slept Score: Baseline (n=69, 78)	0.5 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 4 (n=31, 51)	0.6 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 8 (n=36, 50)	0.7 (± 0.47)	0.6 (± 0.49)		
Optimal Hours Slept Score: Week 12 (n=32, 49)	0.4 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 16 (n=42, 52)	0.5 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 20 (n=21, 21)	0.7 (± 0.46)	0.5 (± 0.51)		
Optimal Hours Slept Score: Week 24 (n=37, 47)	0.4 (± 0.50)	0.5 (± 0.51)		
Optimal Hours Slept Score: Week 28 (n=18, 17)	0.4 (± 0.51)	0.5 (± 0.51)		
Optimal Hours Slept Score: Week 32 (n=34, 45)	0.5 (± 0.51)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 36 (n=17, 17)	0.5 (± 0.51)	0.6 (± 0.51)		
Optimal Hours Slept Score: Week 40 (n=34, 47)	0.5 (± 0.51)	0.4 (± 0.49)		
Optimal Hours Slept Score: Week 44 (n=18, 17)	0.6 (± 0.51)	0.7 (± 0.47)		
Optimal Hours Slept Score: Week 48 (n=30, 43)	0.6 (± 0.50)	0.4 (± 0.50)		
Optimal Hours Slept Score: Week 52 (n=32, 43)	0.4 (± 0.49)	0.5 (± 0.51)		
Short of B or H score: Baseline(n=69, 78)	24.1 (± 9.44)	27.2 (± 15.45)		
Short of B or H score: Week 4 (n=32, 51)	23.8 (± 11.85)	23.9 (± 9.81)		
Short of B or H score: Week 8 (n=36, 50)	24.4 (± 10.81)	25.2 (± 12.66)		
Short of B or H score: Week 12 (n=32, 49)	25.0 (± 10.16)	26.5 (± 13.16)		
Short of B or H score: Week 16 (n=42, 52)	26.2 (± 12.87)	25.0 (± 11.11)		
Short of B or H score: Week 20 (n=21, 21)	24.8 (± 10.78)	29.5 (± 18.57)		
Short of B or H score: Week 24 (n=37, 47)	27.6 (± 15.88)	27.7 (± 13.55)		
Short of B or H score: Week 28 (n=18, 17)	27.8 (± 19.57)	29.4 (± 18.86)		
Short of B or H score: Week 32 (n=34, 45)	26.5 (± 12.76)	23.1 (± 10.41)		

Short of B or H score: Week 36 (n=17, 17)	25.9 (± 11.76)	23.5 (± 14.55)		
Short of B or H score: Week 40 (n=34, 47)	25.3 (± 12.37)	26.0 (± 13.13)		
Short of B or H score: Week 44 (n=18, 17)	28.9 (± 17.11)	27.1 (± 14.04)		
Short of B or H score: Week 48 (n=30, 43)	25.3 (± 11.67)	26.5 (± 14.29)		
Short of B or H score: Week 52 (n=32, 43)	1.3 (± 12.38)	-0.5 (± 16.61)		
Snoring Score: Baseline (n=69, 78)	42.9 (± 26.41)	37.2 (± 23.40)		
Snoring Score: Week 4 (n=32, 51)	46.9 (± 27.17)	36.5 (± 21.43)		
Snoring Score: Week 8 (n=36, 50)	47.2 (± 26.25)	36.8 (± 22.99)		
Snoring Score: Week 12 (n=32, 49)	45.6 (± 27.93)	34.7 (± 21.12)		
Snoring Score: Week 16 (n=42, 52)	43.3 (± 24.96)	35.0 (± 20.15)		
Snoring Score: Week 20 (n=21, 21)	41.9 (± 27.50)	30.5 (± 17.46)		
Snoring Score: Week 24 (n=37, 47)	50.3 (± 27.74)	39.6 (± 24.13)		
Snoring Score: Week 28 (n=18, 17)	45.6 (± 28.95)	31.8 (± 21.28)		
Snoring Score: Week 32 (n=34, 45)	42.4 (± 24.50)	39.1 (± 22.55)		
Snoring Score: Week 36 (n=17, 17)	37.6 (± 21.07)	31.8 (± 18.79)		
Snoring Score: Week 40 (n=34, 47)	44.1 (± 26.87)	37.4 (± 21.52)		
Snoring Score: Week 44 (n=18, 17)	36.7 (± 24.97)	34.1 (± 19.70)		
Snoring Score: Week 48 (n=30, 43)	44.0 (± 22.53)	37.2 (± 23.74)		
Snoring Score: Week 52 (n=32, 43)	45.6 (± 23.41)	37.2 (± 22.07)		
Sleep Disturbance Score: Baseline (n=69, 78)	38.3 (± 18.74)	34.8 (± 17.51)		
Sleep Disturbance Score: Week 4 (n=32, 51)	33.7 (± 15.01)	32.2 (± 14.92)		
Sleep Disturbance Score: Week 8 (n=36, 50)	32.9 (± 13.80)	35.3 (± 15.70)		
Sleep Disturbance Score: Week 12 (n=32, 49)	35.1 (± 16.20)	32.8 (± 16.90)		
Sleep Disturbance Score: Week 16 (n=42, 52)	38.6 (± 19.44)	30.8 (± 15.43)		
Sleep Disturbance Score: Week 20 (n=21, 21)	38.7 (± 22.89)	32.1 (± 13.85)		
Sleep Disturbance Score: Week 24 (n=37, 47)	32.2 (± 19.95)	36.3 (± 18.02)		
Sleep Disturbance Score: Week 28 (n=18, 17)	39.3 (± 22.69)	37.2 (± 16.40)		
Sleep Disturbance Score: Week 32 (n=34, 45)	34.2 (± 20.09)	32.0 (± 14.20)		
Sleep Disturbance Score: Week 36 (n=17, 17)	38.2 (± 23.61)	32.2 (± 16.82)		
Sleep Disturbance Score: Week 40 (n=34, 47)	34.7 (± 18.96)	33.0 (± 16.83)		
Sleep Disturbance Score: Week 44 (n=18, 17)	32.9 (± 23.13)	38.9 (± 16.87)		
Sleep Disturbance Score: Week 48 (n=30, 43)	36.3 (± 18.59)	32.1 (± 16.29)		
Sleep Disturbance Score: Week 52 (n=32, 43)	35.9 (± 19.59)	32.9 (± 17.59)		
Sleep Adequacy Score: Baseline (n=69, 78)	68.6 (± 18.25)	69.1 (± 21.69)		
Sleep Adequacy Score: Week 4 (n=32, 51)	70.6 (± 20.15)	71.6 (± 18.80)		
Sleep Adequacy Score: Week 8 (n=36, 50)	72.5 (± 16.45)	72.6 (± 20.58)		

Sleep Adequacy Score: Week 12 (n=32, 49)	71.9 (± 22.92)	68.2 (± 21.47)		
Sleep Adequacy Score: Week 16 (n=42, 52)	73.3 (± 20.20)	69.0 (± 18.71)		
Sleep Adequacy Score: Week 20 (n=21, 21)	70.5 (± 21.56)	67.6 (± 17.86)		
Sleep Adequacy Score: Week 24 (n=37, 47)	71.6 (± 21.02)	67.4 (± 20.59)		
Sleep Adequacy Score: Week 28 (n=18, 17)	71.7 (± 22.03)	71.2 (± 21.47)		
Sleep Adequacy Score: Week 32 (n=34, 45)	74.7 (± 21.21)	72.4 (± 19.67)		
Sleep Adequacy Score: Week 36 (n=17, 17)	74.1 (± 22.38)	68.8 (± 15.76)		
Sleep Adequacy Score: Week 40 (n=34, 47)	68.5 (± 21.34)	69.1 (± 18.51)		
Sleep Adequacy Score: Week 44 (n=18, 17)	72.2 (± 22.90)	70.0 (± 21.79)		
Sleep Adequacy Score: Week 48 (n=30, 43)	73.0 (± 18.96)	70.2 (± 19.70)		
Sleep Adequacy Score: Week 52 (n=32, 43)	70.0 (± 20.48)	68.6 (± 22.74)		
Sleep Somnolence Score: Baseline (n= 69, 78)	40.3 (± 17.05)	41.8 (± 18.51)		
Sleep Somnolence Score: Week 4 (n=32, 51)	39.6 (± 15.23)	42.4 (± 18.13)		
Sleep Somnolence Score: Week 8 (n=36, 50)	36.5 (± 10.75)	40.1 (± 18.78)		
Sleep Somnolence Score: Week 12 (n=32, 49)	41.7 (± 18.86)	40.4 (± 18.48)		
Sleep Somnolence Score: Week 16 (n=42, 52)	37.1 (± 16.00)	39.1 (± 17.06)		
Sleep Somnolence Score: Week 20 (n=21, 21)	41.3 (± 19.62)	37.5 (± 17.82)		
Sleep Somnolence Score: Week 24 (n=37, 47)	39.5 (± 17.02)	43.4 (± 18.06)		
Sleep Somnolence Score: Week 28 (n=18, 17)	44.4 (± 21.57)	41.2 (± 19.33)		
Sleep Somnolence Score: Week 32 (n=34, 45)	43.7 (± 21.16)	41.5 (± 15.63)		
Sleep Somnolence Score: Week 36 (n=17, 17)	34.9 (± 17.41)	39.2 (± 14.70)		
Sleep Somnolence Score: Week 40 (n=34, 47)	38.6 (± 17.96)	43.3 (± 14.70)		
Sleep Somnolence Score: Week 44 (n=18, 17)	39.3 (± 17.84)	44.3 (± 16.99)		
Sleep Somnolence Score: Week 48 (n=30, 43)	41.3 (± 15.40)	42.3 (± 13.48)		
Sleep Somnolence Score: Week 52 (n=32, 43)	-1.3 (± 15.92)	-4.0 (± 19.90)		
Sleep Problems Index I Score: Baseline (n=69, 78)	33.4 (± 12.63)	33.2 (± 14.19)		
Sleep Problems Index I Score: Week 4 (n=32, 51)	31.4 (± 13.22)	31.6 (± 11.53)		
Sleep Problems Index I Score: Week 8 (n=36, 50)	29.6 (± 10.77)	31.5 (± 13.98)		
Sleep Problems Index I Score: Week 12 (n=32, 49)	32.2 (± 14.36)	33.3 (± 12.89)		
Sleep Problems Index I Score: Week 16 (n=42, 52)	32.1 (± 14.44)	31.8 (± 12.14)		
Sleep Problems Index I Score: Week 20 (n=21, 21)	34.0 (± 16.21)	32.9 (± 13.01)		

Sleep Problems Index I Score: Week 24 (n=37, 47)	30.9 (± 14.92)	34.6 (± 13.63)		
Sleep Problems Index I Score: Week 28 (n=18, 17)	34.4 (± 18.22)	32.9 (± 13.74)		
Sleep Problems Index I Score: Week 32 (n=34, 45)	31.7 (± 14.10)	30.5 (± 11.72)		
Sleep Problems Index I Score: Week 36 (n=17, 17)	31.4 (± 18.11)	31.6 (± 12.86)		
Sleep Problems Index I Score: Week 40 (n=34, 47)	33.0 (± 15.07)	33.7 (± 13.55)		
Sleep Problems Index I Score: Week 44 (n=18, 17)	32.4 (± 18.32)	33.5 (± 13.25)		
Sleep Problems Index I Score: Week 48 (n=30, 43)	33.3 (± 15.06)	32.0 (± 12.20)		
Sleep Problems Index I Score: Week 52 (n=32, 43)	32.4 (± 13.92)	32.6 (± 14.08)		
Sleep Problems Index II Score: Baseline (n=69, 78)	35.5 (± 13.20)	34.4 (± 14.17)		
Sleep Problems Index II Score: Week 4 (n=32, 51)	32.6 (± 11.70)	32.1 (± 11.57)		
Sleep Problems Index II Score: Week 8 (n=36, 50)	31.4 (± 10.70)	33.1 (± 13.16)		
Sleep Problems Index II Score: Week 12 (n=32, 49)	33.2 (± 14.40)	33.2 (± 13.21)		
Sleep Problems Index II Score: Week 16 (n=42, 52)	33.9 (± 15.58)	32.0 (± 11.95)		
Sleep Problems Index II Score: Week 20 (n=21, 21)	35.9 (± 17.75)	33.1 (± 11.87)		
Sleep Problems Index II Score: Week 24 (n=37, 47)	32.1 (± 15.49)	35.9 (± 13.54)		
Sleep Problems Index II Score: Week 28 (n=18, 17)	36.7 (± 18.79)	35.0 (± 13.07)		
Sleep Problems Index II Score: Week 32 (n=34, 45)	33.5 (± 14.89)	31.6 (± 11.07)		
Sleep Problems Index II Score: Week 36 (n=17, 17)	33.5 (± 19.04)	32.2 (± 12.20)		
Sleep Problems Index II Score: Week 40 (n=34, 47)	33.7 (± 15.62)	33.9 (± 12.86)		
Sleep Problems Index II Score: Week 44 (n=18,17)	33.0 (± 18.97)	36.9 (± 13.73)		
Sleep Problems Index II Score: Week 48 (n=30, 43)	33.7 (± 15.44)	32.9 (± 12.13)		
Sleep Problems Index II Score: Week 52 (n=32, 43)	33.8 (± 14.86)	33.0 (± 13.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Outcomes Study Sleep Scale Score: First Flare Period

End point title	Medical Outcomes Study Sleep Scale Score: First Flare Period

End point description:

The MOS Sleep Scale is a 12-item measure that is segregated into subscales addressing seven sleep domains (i.e. sleep disturbance, snoring, short of breath or headache, adequacy of sleep, somnolence, sleep problems index I and sleep problems index II). An additional single item assessed quantity of sleep. The sleep domains and problems index I and problems index II were scored on a range of 0-100, and higher scores indicated worse outcomes. The quantity of sleep scores ranged from 0 to 24 (number of hours slept). The optimal sleep sub-scale score is a binary outcome derived from SQ: the response is

Yes (or 1) if SQ= 7 or 8 hours per night. Observed scores for each individual sleep domain and quantity of sleep are reported in this end point. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary
End point timeframe:	
Weeks 0, 4, 8 and 12	

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Quantity Hours Slept Score: Week 0 (n=42, 44)	7.3 (± 2.28)	7.6 (± 3.56)		
Quantity Hours Slept Score: Week 4 (n=21, 24)	8.2 (± 3.88)	7.3 (± 1.55)		
Quantity Hours Slept Score: Week 8 (n=13, 15)	8.3 (± 3.45)	6.9 (± 1.68)		
Quantity Hours Slept Score: Week 12 (n=3, 7)	8.0 (± 1.00)	7.3 (± 1.70)		
Optimal Hours Slept Score: Week 0 (n=42, 44)	0.6 (± 0.49)	0.4 (± 0.50)		
Optimal Hours Slept Score: Week 4 (n=21, 24)	0.5 (± 0.51)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 8 (n=13, 15)	0.5 (± 0.52)	0.5 (± 0.52)		
Optimal Hours Slept Score: Week 12 (n=3, 7)	0.7 (± 0.58)	0.4 (± 0.53)		
Short of B or H score: Week 0 (n=43, 44)	27.9 (± 16.98)	28.6 (± 17.47)		
Short of B or H score: Week 4 (n=21, 24)	26.7 (± 13.17)	27.5 (± 14.22)		
Short of B or H score: Week 8 (n=13, 15)	27.7 (± 15.36)	33.3 (± 19.52)		
Short of B or H score: Week 12 (n=3, 7)	20.0 (± 0.00)	22.9 (± 7.56)		
Snoring Score: Week 0 (n=43, 44)	43.3 (± 28.26)	37.7 (± 24.86)		
Snoring Score: Week 4 (n=21, 24)	45.7 (± 28.39)	39.2 (± 27.96)		
Snoring Score: Week 8 (n=13, 15)	44.6 (± 24.70)	38.7 (± 23.26)		
Snoring Score: Week 12 (n=3, 7)	53.3 (± 23.09)	34.3 (± 19.02)		
Sleep Disturbance Score: Week 0 (n=43, 44)	41.0 (± 19.08)	40.9 (± 19.39)		
Sleep Disturbance Score: Week 4 (n=21, 24)	38.3 (± 18.36)	38.6 (± 18.61)		
Sleep Disturbance Score: Week 8 (n=13, 15)	33.6 (± 12.81)	41.4 (± 16.77)		
Sleep Disturbance Score: Week 12 (n=3, 7)	43.3 (± 16.65)	43.6 (± 13.02)		
Sleep Adequacy Score: Week 0 (n=43, 44)	67.0 (± 20.99)	66.1 (± 20.71)		
Sleep Adequacy Score: Week 4 (n=21, 24)	71.0 (± 23.00)	67.1 (± 24.22)		
Sleep Adequacy Score: Week 8 (n=13, 15)	70.0 (± 22.36)	66.0 (± 19.20)		
Sleep Adequacy Score: Week 12 (n=3, 7)	76.7 (± 15.28)	64.3 (± 17.18)		

Sleep Somnolence Score: Week 0 (n=43, 44)	44.8 (± 20.74)	45.9 (± 19.30)		
Sleep Somnolence Score: Week 4 (n=21, 24)	42.9 (± 22.76)	48.3 (± 19.49)		
Sleep Somnolence Score: Week 8 (n=13, 15)	45.6 (± 22.91)	54.2 (± 19.17)		
Sleep Somnolence Score: Week 12 (n=3, 7)	33.3 (± 13.33)	50.5 (± 19.57)		
Sleep Problems Index I Score: Week 0 (n=43, 44)	36.3 (± 13.53)	37.3 (± 15.29)		
Sleep Problems Index I Score: Week 4 (n=21, 24)	32.9 (± 16.27)	36.7 (± 16.33)		
Sleep Problems Index I Score: Week 8 (n=13, 15)	32.8 (± 9.51)	38.9 (± 13.07)		
Sleep Problems Index I Score: Week 12 (n=3, 7)	31.1 (± 11.71)	39.0 (± 5.35)		
Sleep Problems Index II Score: Baseline (n=43, 44)	38.4 (± 14.19)	38.6 (± 15.55)		
Sleep Problems Index II Score: Week 4 (n=21, 24)	35.8 (± 16.81)	38.0 (± 16.06)		
Sleep Problems Index II Score: Week 8 (n=13, 15)	34.6 (± 10.26)	41.4 (± 13.30)		
Sleep Problems Index II Score: Week 12 (n=3, 7)	34.1 (± 12.97)	40.3 (± 6.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Outcomes Study Sleep Scale Score: First Flare Free Period

End point title	Medical Outcomes Study Sleep Scale Score: First Flare Free Period

End point description:

The MOS Sleep Scale is a 12-item measure that is segregated into subscales addressing seven sleep domains (i.e. sleep disturbance, snoring, short of breath or headache, adequacy of sleep, somnolence, sleep problems index I and sleep problems index II). An additional single item assessed quantity of sleep. The sleep domains and problems index I and problems index II were scored on a range of 0-100, and higher scores indicated worse outcomes. The quantity of sleep scores ranged from 0 to 24 (number of hours slept). The optimal sleep sub-scale score is a binary outcome derived from SQ: the response is Yes (or 1) if SQ= 7 or 8 hours per night. Observed scores for each individual sleep domain and quantity of sleep are reported in this end point. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Quantity Hours Slept Score: Baseline (n=69, 78)	8.3 (± 3.79)	7.5 (± 2.42)		
Quantity Hours Slept Score: Week 4 (n=29, 51)	9.0 (± 4.68)	8.1 (± 3.32)		
Quantity Hours Slept Score: Week 8 (n=25, 44)	8.5 (± 3.77)	7.9 (± 3.92)		
Quantity Hours Slept Score: Week 12 (n=20, 40)	8.6 (± 4.15)	7.6 (± 3.22)		
Quantity Hours Slept Score: Week 16 (n=19, 37)	8.5 (± 4.11)	8.5 (± 4.90)		
Quantity Hours Slept Score: Week 20 (n=8, 13)	7.0 (± 1.20)	7.7 (± 1.55)		
Quantity Hours Slept Score: Week 24 (n=17, 31)	7.2 (± 1.99)	7.4 (± 3.45)		
Quantity Hours Slept Score: Week 28 (n=7, 9)	6.9 (± 1.07)	7.4 (± 1.51)		
Quantity Hours Slept Score: Week 32 (n=16, 27)	8.5 (± 4.24)	7.6 (± 1.22)		
Quantity Hours Slept Score: Week 36 (n=6, 7)	7.0 (± 0.89)	8.0 (± 1.41)		
Quantity Hours Slept Score: Week 40 (n=17, 26)	8.3 (± 4.57)	7.5 (± 2.97)		
Quantity Hours Slept Score: Week 44 (n=7, 9)	6.7 (± 1.11)	7.1 (± 0.60)		
Quantity Hours Slept Score: Week 48 (n=17, 24)	7.2 (± 1.63)	7.2 (± 1.46)		
Quantity Hours Slept Score: Week 52 (n=15, 23)	8.0 (± 4.57)	7.0 (± 1.24)		
Optimal Hours Slept Score: Baseline (n=69, 78)	0.5 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 4 (n=29, 51)	0.6 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 8 (n=25, 44)	0.7 (± 0.46)	0.6 (± 0.49)		
Optimal Hours Slept Score: Week 12 (n=20, 40)	0.4 (± 0.50)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 16 (n=19, 37)	0.5 (± 0.51)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 20 (n=8, 13)	0.6 (± 0.52)	0.5 (± 0.52)		
Optimal Hours Slept Score: Week 24 (n=17, 31)	0.5 (± 0.51)	0.6 (± 0.50)		
Optimal Hours Slept Score: Week 28 (n=7, 9)	0.7 (± 0.49)	0.6 (± 0.53)		
Optimal Hours Slept Score: Week 32 (n=16, 27)	0.6 (± 0.50)	0.7 (± 0.45)		
Optimal Hours Slept Score: Week 36 (n=6, 7)	0.7 (± 0.52)	0.9 (± 0.38)		
Optimal Hours Slept Score: Week 40 (n=17, 26)	0.5 (± 0.51)	0.5 (± 0.51)		
Optimal Hours Slept Score: Week 44 (n=7, 9)	0.6 (± 0.53)	0.9 (± 0.33)		
Optimal Hours Slept Score: Week 48 (n=17, 24)	0.6 (± 0.51)	0.4 (± 0.50)		

Optimal Hours Slept Score: Week 52 (n=15, 23)	0.4 (± 0.51)	0.5 (± 0.51)		
Short of B or H score: Baseline (n=69, 78)	24.1 (± 9.44)	27.2 (± 15.45)		
Short of B or H score:Week 4 (n=30, 51)	24.0 (± 12.21)	23.9 (± 9.81)		
Short of B or H score: Week 8 (n=25, 44)	24.8 (± 10.46)	23.6 (± 9.90)		
Short of B or H score: Week 12 (n=20, 40)	23.0 (± 7.33)	26.0 (± 12.97)		
Short of B or H score: Week 16 (n=19, 37)	24.2 (± 8.38)	24.9 (± 10.96)		
Short of B or H score: Week 20 (n=8, 13)	22.5 (± 7.07)	29.2 (± 17.54)		
Short of B or H score: Week 24 (n=17, 31)	24.7 (± 11.25)	26.5 (± 11.99)		
Short of B or H score: Week 28 (n=7, 9)	31.4 (± 22.68)	26.7 (± 14.14)		
Short of B or H score: Week 32 (n=16, 27)	25.0 (± 8.94)	22.2 (± 8.47)		
Short of B or H score: Week 36 (n=6, 7)	20.0 (± 0.00)	20.0 (± 0.00)		
Short of B or H score: Week 40 (n=17, 26)	22.4 (± 6.64)	25.4 (± 12.08)		
Short of B or H score: Week 44 (n=7, 9)	22.9 (± 7.56)	28.9 (± 14.53)		
Short of B or H score: Week 48 (n=17, 24)	22.4 (± 6.64)	25.0 (± 12.16)		
Short of B or H score: Week 52 (n=15, 23)	22.7 (± 7.04)	27.8 (± 11.66)		
Snoring Score: Baseline (n=69, 78)	42.9 (± 26.41)	37.2 (± 23.40)		
Snoring Score: Week 4 (n=30, 51)	47.3 (± 27.53)	36.5 (± 21.43)		
Snoring Score: Week 8 (n=25, 44)	49.6 (± 26.53)	35.5 (± 22.77)		
Snoring Score: Week 12 (n=20, 40)	49.0 (± 28.64)	33.5 (± 20.95)		
Snoring Score: Week 16 (n=19, 37)	45.3 (± 27.36)	34.6 (± 19.80)		
Snoring Score: Week 20 (n=8, 13)	42.5 (± 27.12)	23.1 (± 7.51)		
Snoring Score: Week 24 (n=17, 31)	54.1 (± 26.23)	38.1 (± 22.72)		
Snoring Score: Week 28 (n=7, 9)	48.6 (± 30.24)	22.2 (± 6.67)		
Snoring Score: Week 32 (n=16, 27)	40.0 (± 19.32)	37.8 (± 21.72)		
Snoring Score: Week 36 (n=6, 7)	36.7 (± 15.06)	25.7 (± 9.76)		
Snoring Score: Week 40 (n=17, 26)	44.7 (± 26.01)	38.5 (± 21.85)		
Snoring Score: Week 44 (n=7, 9)	28.6 (± 10.69)	28.9 (± 14.53)		
Snoring Score: Week 48 (n=17, 24)	44.7 (± 16.63)	40.0 (± 24.32)		
Snoring Score: Week 52 (n=15, 23)	46.7 (± 20.93)	41.7 (± 21.67)		
Sleep Disturbance Score: Baseline (n=69, 78)	38.3 (± 18.74)	34.8 (± 17.51)		
Sleep Disturbance Score: Week 4 (n=30, 51)	34.3 (± 15.11)	32.2 (± 14.92)		
Sleep Disturbance Score: Week 8 (n=25, 44)	31.7 (± 12.00)	35.1 (± 16.27)		
Sleep Disturbance Score: Week 12 (n=20, 40)	33.3 (± 14.51)	32.3 (± 17.12)		
Sleep Disturbance Score: Week 16 (n=19, 37)	35.9 (± 17.17)	30.6 (± 14.57)		
Sleep Disturbance Score: Week 20 (n=8, 13)	32.8 (± 12.22)	28.0 (± 9.31)		
Sleep Disturbance Score: Week 24 (n=17, 31)	30.7 (± 15.90)	35.9 (± 18.34)		
Sleep Disturbance Score: Week 28 (n=7, 9)	37.3 (± 11.78)	31.1 (± 12.43)		
Sleep Disturbance Score: Week 32 (n=16, 27)	31.4 (± 14.75)	32.3 (± 12.28)		

Sleep Disturbance Score: Week 36 (n=6, 7)	27.7 (± 9.43)	27.7 (± 10.93)		
Sleep Disturbance Score: Week 40 (n=17, 26)	34.3 (± 14.80)	33.2 (± 18.06)		
Sleep Disturbance Score: Week 44 (n=7, 9)	23.9 (± 10.47)	34.3 (± 16.25)		
Sleep Disturbance Score: Week 48 (n=17, 24)	33.9 (± 11.81)	30.2 (± 16.76)		
Sleep Disturbance Score: Week 52 (n=15, 23)	32.4 (± 16.27)	31.6 (± 15.29)		
Sleep Adequacy Score: Baseline (n=69, 78)	68.6 (± 18.25)	69.1 (± 21.69)		
Sleep Adequacy Score: Week 4 (n=30, 51)	71.0 (± 20.74)	71.6 (± 18.80)		
Sleep Adequacy Score: Week 8 (n=25, 44)	72.8 (± 17.20)	73.2 (± 21.43)		
Sleep Adequacy Score: Week 12 (n=20, 40)	75.0 (± 20.90)	68.0 (± 21.74)		
Sleep Adequacy Score: Week 16 (n=19, 37)	74.7 (± 20.65)	66.5 (± 17.98)		
Sleep Adequacy Score: Week 20 (n=8, 13)	70.0 (± 22.68)	66.9 (± 21.36)		
Sleep Adequacy Score: Week 24 (n=17, 31)	76.5 (± 16.18)	68.1 (± 20.88)		
Sleep Adequacy Score: Week 28 (n=7, 9)	70.0 (± 19.15)	72.2 (± 28.19)		
Sleep Adequacy Score: Week 32 (n=16, 27)	78.8 (± 14.55)	74.4 (± 19.87)		
Sleep Adequacy Score: Week 36 (n=6, 7)	75.0 (± 15.17)	72.9 (± 17.99)		
Sleep Adequacy Score: Week 40 (n=17, 26)	72.9 (± 16.11)	68.1 (± 18.33)		
Sleep Adequacy Score: Week 44 (n=7, 9)	67.1 (± 26.28)	73.3 (± 26.46)		
Sleep Adequacy Score: Week 48 (n=17, 24)	75.3 (± 14.63)	72.9 (± 18.99)		
Sleep Adequacy Score: Week 52 (n=15, 23)	74.7 (± 13.56)	67.8 (± 23.35)		
Sleep Somnolence Score: Baseline (n=69, 78)	40.3 (± 17.05)	41.8 (± 18.51)		
Sleep Somnolence Score: Week 4 (n=30, 51)	40.0 (± 15.56)	42.4 (± 18.13)		
Sleep Somnolence Score: Week 8 (n=25, 44)	36.3 (± 10.55)	39.1 (± 18.89)		
Sleep Somnolence Score: Week 12 (n=20, 40)	38.0 (± 14.03)	41.3 (± 18.81)		
Sleep Somnolence Score: Week 16 (n=19, 37)	34.4 (± 10.00)	40.5 (± 17.38)		
Sleep Somnolence Score: Week 20 (n=8, 13)	42.5 (± 24.67)	36.9 (± 20.66)		
Sleep Somnolence Score: Week 24 (n=17, 31)	39.6 (± 16.07)	42.8 (± 19.98)		
Sleep Somnolence Score: Week 28 (n=7, 9)	48.6 (± 24.26)	37.0 (± 20.03)		
Sleep Somnolence Score: Week 32 (n=16, 27)	44.6 (± 20.76)	42.5 (± 15.04)		
Sleep Somnolence Score: Week 36 (n=6, 7)	35.6 (± 19.63)	31.4 (± 9.20)		
Sleep Somnolence Score: Week 40 (n=17, 26)	36.1 (± 16.51)	43.1 (± 15.35)		
Sleep Somnolence Score: Week 44 (n=7, 9)	37.1 (± 16.71)	40.7 (± 18.99)		

Sleep Somnolence Score: Week 48 (n=17, 24)	39.6 (± 14.62)	43.1 (± 13.04)		
Sleep Somnolence Score: Week 52 (n=15, 23)	38.7 (± 13.14)	39.1 (± 14.11)		
Sleep Problems Index I Score: Baseline (n=69, 78)	33.4 (± 12.63)	33.2 (± 14.19)		
Sleep Problems Index I Score: Week 4 (n=30, 51)	31.4 (± 13.64)	31.6 (± 11.53)		
Sleep Problems Index I Score: Week 8 (n=25, 44)	28.9 (± 10.79)	30.7 (± 13.99)		
Sleep Problems Index I Score: Week 12 (n=20, 40)	29.3 (± 13.27)	33.2 (± 13.22)		
Sleep Problems Index I Score: Week 16 (n=19, 37)	30.2 (± 11.78)	32.6 (± 12.10)		
Sleep Problems Index I Score: Week 20 (n=8, 13)	32.5 (± 12.05)	31.8 (± 14.12)		
Sleep Problems Index I Score: Week 24 (n=17, 31)	28.0 (± 12.25)	34.4 (± 14.87)		
Sleep Problems Index I Score: Week 28 (n=7, 9)	35.7 (± 13.97)	28.5 (± 13.34)		
Sleep Problems Index I Score: Week 32 (n=16, 27)	29.2 (± 8.39)	30.5 (± 12.63)		
Sleep Problems Index I Score: Week 36 (n=6, 7)	28.3 (± 9.83)	26.2 (± 11.45)		
Sleep Problems Index I Score: Week 40 (n=17, 26)	30.8 (± 11.15)	34.4 (± 14.78)		
Sleep Problems Index I Score: Week 44 (n=7, 9)	29.5 (± 11.93)	30.7 (± 14.32)		
Sleep Problems Index I Score: Week 48 (n=17, 24)	31.6 (± 10.74)	31.0 (± 12.83)		
Sleep Problems Index I Score: Week 52 (n=15, 23)	30.2 (± 9.13)	32.0 (± 13.62)		
Sleep Problems Index II Score: Baseline (n=69, 78)	35.5 (± 13.20)	34.4 (± 14.17)		
Sleep Problems Index II Score: Week 4 (n=30, 51)	32.8 (± 12.00)	32.1 (± 11.57)		
Sleep Problems Index II Score: Week 8 (n=25, 44)	30.3 (± 10.27)	32.4 (± 13.36)		
Sleep Problems Index II Score: Week 12 (n=20, 40)	30.5 (± 12.70)	32.8 (± 13.47)		
Sleep Problems Index II Score: Week 16 (n=19, 37)	31.2 (± 12.90)	32.7 (± 11.83)		
Sleep Problems Index II Score: Week 20 (n=8, 13)	33.2 (± 12.21)	31.1 (± 11.85)		
Sleep Problems Index II Score: Week 24 (n=17, 31)	29.6 (± 11.67)	35.4 (± 14.29)		
Sleep Problems Index II Score: Week 28 (n=7, 9)	36.9 (± 12.41)	30.9 (± 11.08)		
Sleep Problems Index II Score: Week 32 (n=16, 27)	30.9 (± 8.47)	31.5 (± 11.36)		
Sleep Problems Index II Score: Week 36 (n=6, 7)	27.9 (± 8.99)	27.5 (± 8.80)		
Sleep Problems Index II Score: Week 40 (n=17, 26)	31.3 (± 10.00)	34.3 (± 14.03)		
Sleep Problems Index II Score: Week 44 (n=7, 9)	28.1 (± 9.82)	33.8 (± 14.04)		
Sleep Problems Index II Score: Week 48 (n=17, 24)	31.4 (± 9.57)	31.6 (± 12.65)		
Sleep Problems Index II Score: Week 52 (n=15, 23)	30.6 (± 8.85)	32.4 (± 12.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life-5 Dimension 5-Level (EuroQoL EQ-5D-5L) Index Score in Subjects Greater Than or Equal to (>=) 18 Years of age: OL Run-in Period

End point title	European Quality of Life-5 Dimension 5-Level (EuroQoL EQ-5D-5L) Index Score in Subjects Greater Than or Equal to (>=) 18 Years of age: OL Run-in Period

End point description:

EQ-5D-5L:subject rated questionnaire consist of 6 questions used to calculate health utility score.Two components to EQ-5D-5L: 5-item health state profile assessed 5 dimensions:mobility,self-care,usual activities,pain/discomfort,anxiety/depression used to obtain Index Utility Score, VAS measures health state. Each dimension:5 levels:1=no problems,2= slight,3= moderate,4= severe,5= extreme. Responses to 5 dimensions comprised health state/a single utility index value.Eg.If subject responded"no problems"for each 5 dimensions,then health state coded:"11111" with predefined index value to it.Health state(coded as combination of responses on 5 dimensions)had unique predefined utility index value assigned to it,by EuroQol. US value sets(with all possible health states)was used for adults in the study,range from1 to-0.109. Higher(positive)scores= better health state.Eval-OL analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	169			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=166)	0.9 (± 0.12)			
Week 2 (n=168)	0.9 (± 0.13)			
Week 4 (n=169)	0.9 (± 0.11)			
Week 6 (n=169)	0.9 (± 0.12)			
Week 8 (n=169)	0.9 (± 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life-5 Dimension Youth (EuroQoL EQ-5D Y) Index Score in Subjects Between 8-17 Years of age: OL Run-in Period

End point title	European Quality of Life-5 Dimension Youth (EuroQoL EQ-5D Y) Index Score in Subjects Between 8-17 Years of age: OL Run-in

	Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	169			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=164)	0.9 (± 0.13)			
Week 2 (n=168)	0.9 (± 0.11)			
Week 4 (n=169)	0.9 (± 0.12)			
Week 6 (n=169)	0.9 (± 0.11)			
Week 8 (n=169)	0.9 (± 0.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: OL Run-in Period

End point title	EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: OL Run-in Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	0.8 (± 0.17)			
Week 2	0.9 (± 0.16)			
Week 4	0.9 (± 0.17)			
Week 6	0.9 (± 0.17)			
Week 8	0.9 (± 0.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L Visual Analog Scale (VAS) Score in Subjects >= 18 Years of age: OL Run-in Period

End point title	EuroQoL EQ-5D-5L Visual Analog Scale (VAS) Score in Subjects >= 18 Years of age: OL Run-in Period

End point description:

The EQ-5D-5L is a participant rated questionnaire that consisted of six questions used to calculate a health utility score. There were two components to the EQ-5D-5L: a five-item health state profile that assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS that measures health state. EQ-5D VAS was used to record subject's rating for his/her current health-related quality of life state on a vertical VAS (0-100), where 0 = worst imaginable health state and 100 = best imaginable health state. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	169			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=166)	81.2 (± 15.81)			
Week 2 (n=168)	82.2 (± 16.14)			
Week 4 (n=169)	82.0 (± 15.73)			
Week 6 (n=169)	84.0 (± 14.89)			
Week 8 (n=169)	84.2 (± 14.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age : OL-Run-in Period

End point title	EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age : OL-Run-in Period

End point description:

The EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Comprised of two components: a five-item health state profile that assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS on which the respondent rated his/her perceived health from 0 (the worst imaginable health) to 100 (the best imaginable health). Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	169			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=164)	85.6 (± 16.27)			
Week 2 (n=168)	87.4 (± 11.91)			
Week 4 (n=169)	87.5 (± 12.92)			
Week 6 (n=169)	87.9 (± 12.72)			
Week 8 (n=169)	88.0 (± 12.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: OL Run-in Period

End point title	EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: OL Run-in Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-OL population included all subjects that received at least 1 dose of study intervention in the OL period. Here, 'N': number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline	86.0 (± 13.97)			
Week 2	87.6 (± 12.61)			
Week 4	90.0 (± 11.05)			
Week 6	90.4 (± 11.45)			
Week 8	90.8 (± 11.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L Index Scores in Subjects >= 18 Years of age: DB Period

End point title	EuroQoL EQ-5D-5L Index Scores in Subjects >= 18 Years of age: DB Period

End point description:

EQ-5D-5L:subject rated questionnaire, 6 questions to calculate health utility score. 2 components to EQ-5D-5L: 5-item health state profile assessed 5 dimensions:mobility,self-care,usual activities,pain/discomfort and anxiety/depression used to obtain Index Utility Score,VAS that measures health state. Each dimension:5 levels:1=no problems,2=slight,3=moderate,4=severe,5=extreme.Response to 5 dimensions comprised health state/a single utility index value.Eg. if subject responded"no problems"for each 5 dimensions, health state coded:"11111" with predefined index value to it.Every health state(coded as combination of responses on each of 5 dimensions):unique predefined utility index value assigned to it by EuroQol. US value sets(with all possible health states)used for adults in the study,range from 1 to -0.109. Higher(positive) scores= better health state. Eval-DB population analysed.'N':number of subjects

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	48		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=46, 48)	0.9 (± 0.09)	0.9 (± 0.11)		
Week 4 (n=23, 30)	0.9 (± 0.12)	0.9 (± 0.10)		
Week 8 (n=25, 31)	0.9 (± 0.09)	0.9 (± 0.10)		
Week 12 (n=23, 28)	0.9 (± 0.10)	0.9 (± 0.18)		

Week 16 (n=31, 33)	0.9 (± 0.11)	0.9 (± 0.15)		
Week 20 (n=15, 13)	0.9 (± 0.12)	0.9 (± 0.15)		
Week 24 (n=26, 30)	0.9 (± 0.10)	0.9 (± 0.21)		
Week 28 (n=12, 11)	0.9 (± 0.18)	0.9 (± 0.14)		
Week 32 (n=23, 27)	0.9 (± 0.11)	0.8 (± 0.22)		
Week 36 (n=11, 11)	0.9 (± 0.09)	0.9 (± 0.13)		
Week 40 (n=23, 28)	0.9 (± 0.10)	0.8 (± 0.24)		
Week 44 (n=12, 11)	0.9 (± 0.18)	0.9 (± 0.14)		
Week 48 (n=22, 24)	0.9 (± 0.11)	0.8 (± 0.23)		
Week 52 (n=25, 23)	0.9 (± 0.10)	0.8 (± 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: DB Period

End point title	EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: DB Period

End point description:

The EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Comprised of two components: a five-item health state profile that assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS on which the respondent rated his/her perceived health from 0 (the worst imaginable health) to 100 (the best imaginable health). Eval-DB population included all randomised subjects with success in ISGA and EASI50 criteria as responders at randomisation and received at least 1 dose of study intervention in the DB period. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	43		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=38, 43)	0.9 (± 0.08)	0.9 (± 0.18)		
Week 4 (n=15, 28)	1.0 (± 0.07)	1.0 (± 0.07)		
Week 8 (n=18, 27)	1.0 (± 0.07)	1.0 (± 0.08)		
Week 12 (n=19, 28)	1.0 (± 0.06)	1.0 (± 0.07)		
Week 16 (n=21, 28)	1.0 (± 0.08)	1.0 (± 0.07)		
Week 20 (n=9, 13)	0.9 (± 0.09)	1.0 (± 0.05)		
Week 24 (n=19, 28)	1.0 (± 0.07)	1.0 (± 0.06)		
Week 28 (n=10, 14)	0.9 (± 0.09)	0.9 (± 0.08)		
Week 32 (n=20, 28)	1.0 (± 0.06)	1.0 (± 0.06)		
Week 36 (n=10, 11)	1.0 (± 0.08)	1.0 (± 0.08)		

Week 40 (n=17, 24)	1.0 (± 0.07)	0.9 (± 0.13)		
Week 44 (n=10, 11)	1.0 (± 0.08)	0.9 (± 0.22)		
Week 48 (n=15, 26)	1.0 (± 0.07)	0.9 (± 0.09)		
Week 52 (n=18, 25)	1.0 (± 0.07)	1.0 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: DB Period

End point title	EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: DB Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	30		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 30)	1.0 (± 0.08)	0.9 (± 0.12)		
Week 4 (n=17, 14)	0.9 (± 0.09)	0.9 (± 0.14)		
Week 8 (n=22, 14)	0.9 (± 0.09)	0.9 (± 0.09)		
Week 12 (n=18, 17)	1.0 (± 0.07)	0.9 (± 0.13)		
Week 16 (n=16, 17)	1.0 (± 0.09)	1.0 (± 0.07)		
Week 20 (n=13, 10)	0.9 (± 0.10)	0.9 (± 0.15)		
Week 24 (n=20, 15)	1.0 (± 0.08)	1.0 (± 0.07)		
Week 28 (n=13, 9)	0.9 (± 0.09)	0.9 (± 0.09)		
Week 32 (n=17, 11)	1.0 (± 0.06)	1.0 (± 0.07)		
Week 36 (n=10, 8)	1.0 (± 0.05)	0.9 (± 0.10)		
Week 40 (n=15, 9)	0.9 (± 0.09)	0.9 (± 0.08)		
Week 44 (n=10, 6)	1.0 (± 0.07)	0.9 (± 0.10)		
Week 48 (n=16, 12)	1.0 (± 0.07)	1.0 (± 0.07)		
Week 52 (n=19, 13)	1.0 (± 0.05)	1.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: DB Period

End point title	EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: DB Period

End point description:

The EQ-5D-5L is a participant rated questionnaire that consisted of six questions used to calculate a health utility score. There were two components to the EQ-5D-5L: a five-item health state profile that assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS that measures health state. EQ-5D VAS was used to record subject's rating for his/her current health-related quality of life state on a vertical VAS (0-100), where 0 = worst imaginable health state and 100 = best imaginable health state. Eval-DB population analysed. Here 'N':number of subjects evaluable for end point,'n':number of subjects evaluable at specific time

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	48		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=46, 48)	88.3 (± 9.41)	85.2 (± 15.56)		
Week 4 (n=23, 30)	89.9 (± 9.00)	86.8 (± 10.74)		
Week 8 (n=25, 31)	90.7 (± 7.76)	87.3 (± 12.02)		
Week 12 (n=23, 28)	88.5 (± 13.72)	80.5 (± 21.68)		
Week 16 (n=31, 33)	88.1 (± 11.86)	82.7 (± 18.94)		
Week 20 (n=15, 13)	87.1 (± 13.77)	82.7 (± 14.47)		
Week 24 (n=26, 30)	89.2 (± 10.98)	83.1 (± 19.39)		
Week 28 (n=12, 11)	88.3 (± 9.29)	83.7 (± 16.57)		
Week 32 (n=23, 27)	90.0 (± 8.91)	83.0 (± 20.02)		
Week 36 (n=11, 11)	90.8 (± 8.68)	83.4 (± 12.80)		
Week 40 (n=23, 28)	88.9 (± 12.99)	82.4 (± 20.68)		
Week 44 (n=12, 11)	87.2 (± 13.64)	81.9 (± 13.96)		
Week 48 (n=22, 24)	88.8 (± 12.90)	85.1 (± 20.92)		
Week 52 (n=25, 23)	90.0 (± 11.44)	82.7 (± 20.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: DB Period

End point title	EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: DB Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	43		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=38, 43)	86.8 (± 14.86)	91.1 (± 9.34)		
Week 4 (n=15, 28)	88.3 (± 11.29)	91.6 (± 7.27)		
Week 8 (n=18, 27)	89.6 (± 9.52)	88.6 (± 14.34)		
Week 12 (n=19, 28)	91.9 (± 9.18)	89.1 (± 13.36)		
Week 16 (n=21, 28)	91.3 (± 8.20)	88.9 (± 13.91)		
Week 20 (n=9, 13)	85.1 (± 10.89)	87.8 (± 21.65)		
Week 24 (n=19, 28)	91.7 (± 10.92)	89.3 (± 12.83)		
Week 28 (n=10, 14)	89.9 (± 12.09)	90.4 (± 13.36)		
Week 32 (n=20, 28)	91.1 (± 9.40)	91.5 (± 12.98)		
Week 36 (n=10, 11)	90.7 (± 10.34)	91.7 (± 14.86)		
Week 40 (n=17, 24)	92.2 (± 9.03)	89.8 (± 13.25)		
Week 44 (n=10, 11)	93.5 (± 8.70)	88.3 (± 15.81)		
Week 48 (n=15, 26)	92.1 (± 9.75)	91.3 (± 13.64)		
Week 52 (n=18, 25)	90.9 (± 13.75)	92.6 (± 11.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: DB Period

End point title	EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7

	Years of age: DB Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period),Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	30		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 30)	93.8 (± 9.97)	94.3 (± 8.16)		
Week 4 (n=17, 14)	94.6 (± 5.86)	96.3 (± 6.54)		
Week 8 (n=22, 14)	93.0 (± 7.39)	96.3 (± 6.17)		
Week 12 (n=18, 17)	95.2 (± 5.47)	96.8 (± 3.73)		
Week 16 (n=16, 17)	92.9 (± 7.08)	96.5 (± 2.81)		
Week 20 (n=13, 10)	94.9 (± 5.09)	93.4 (± 6.50)		
Week 24 (n=20, 15)	95.1 (± 5.62)	95.7 (± 4.62)		
Week 28 (n=13, 9)	95.8 (± 5.60)	97.1 (± 4.17)		
Week 32 (n=17, 11)	95.5 (± 5.70)	96.9 (± 2.12)		
Week 36 (n=10, 8)	97.4 (± 2.99)	97.8 (± 2.49)		
Week 40 (n=15, 9)	93.7 (± 7.76)	96.8 (± 3.46)		
Week 44 (n=10, 6)	96.6 (± 4.60)	97.8 (± 2.71)		
Week 48 (n=16, 12)	96.1 (± 5.15)	96.9 (± 4.01)		
Week 52 (n=19, 13)	95.0 (± 5.51)	96.7 (± 3.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L Index Scores in Subjects >= 18 Years of age: First Flare Period

End point title	EuroQoL EQ-5D-5L Index Scores in Subjects >= 18 Years of age: First Flare Period

End point description:

The EQ-5D-5L is a participant rated questionnaire that consisted of six questions used to calculate a health utility score. There were two components to the EQ-5D-5L: a five-item health state profile that assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS that measures health state. EQ-5D VAS was used to record subject's rating for his/her current health-related quality of life state on a vertical VAS (0-100), where 0

imaginable health state and 100 = best imaginable health state. Eval-DB population analysed. Here 'N':number of subjects evaluable for end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary
End point timeframe:	
Weeks 0, 4, 8 and 12	

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=27, 28)	0.9 (± 0.11)	0.9 (± 0.15)		
Week 4 (n=14, 15)	1.0 (± 0.07)	0.8 (± 0.19)		
Week 8 (n= 9, 10)	1.0 (± 0.06)	0.8 (± 0.07)		
Week 12 (n=3, 3)	0.9 (± 0.10)	0.9 (± 0.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: First Flare Period

End point title	EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: First Flare Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary
End point timeframe:	
Weeks 0, 4, 8 and 12	

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	22		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=28, 22)	0.9 (± 0.09)	0.8 (± 0.25)		
Week 4 (n=14, 13)	0.9 (± 0.09)	0.9 (± 0.13)		

Week 8 (n=9, 9)	0.9 (± 0.10)	0.9 (± 0.11)		
Week 12 (n=1, 5)	1.0 (± 99999)	0.9 (± 0.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: First Flare Period

End point title	EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: First Flare Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	23		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=30, 23)	0.8 (± 0.22)	0.8 (± 0.15)		
Week 4 (n=19, 15)	0.9 (± 0.18)	0.9 (± 0.16)		
Week 8 (n=12, 6)	0.9 (± 0.11)	0.8 (± 0.20)		
Week 12 (n=4, 1)	0.9 (± 0.10)	1.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: First Flare Period

End point title	EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: First Flare Period

End point description:

The EQ-5D-5L is a participant rated questionnaire that consisted of six questions used to calculate a health utility score. There were two components to the EQ-5D-5L: a five-item health state profile that

assessed mobility, self-care, usual activities, pain/discomfort, and anxiety/depression used to obtain an Index Utility Score, as well as a VAS that measures health state. EQ-5D VAS was used to record subject's rating for his/her current health-related quality of life state on a vertical VAS (0-100), where 0 = worst imaginable health state and 100 = best imaginable health state. Eval-DB population was analysed. Here 'N':number of subjects evaluable for end point,'n':number of subjects evaluable at

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=27, 28)	84.1 (± 10.40)	82.8 (± 17.81)		
Week 4 (n=14, 15)	87.9 (± 8.02)	81.1 (± 22.15)		
Week 8 (n=9, 10)	88.6 (± 6.71)	88.2 (± 9.25)		
Week 12 (n=3, 3)	83.7 (± 11.85)	85.0 (± 21.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: First Flare Period

End point title	EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: First Flare Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	22		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=28, 22)	86.5 (± 10.87)	88.7 (± 10.27)		
Week 4 (n=14, 13)	91.5 (± 8.91)	82.3 (± 18.55)		
Week 8 (n=9, 9)	85.3 (± 17.58)	87.0 (± 9.49)		
Week 12 (n=1, 5)	100.0 (± 99999)	81.0 (± 4.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: First Flare Period

End point title	EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: First Flare Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	23		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=30, 23)	84.7 (± 21.55)	91.0 (± 7.84)		
Week 4 (n=19, 15)	90.3 (± 13.53)	91.3 (± 7.69)		
Week 8 (n=12, 6)	93.8 (± 5.29)	93.0 (± 7.90)		
Week 12 (n=4, 1)	90.0 (± 10.61)	99.0 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Index Scores in Subjects >= 18 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D Y Index Scores in Subjects >= 18 Years of age: First Flare Free Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	48		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=46, 48)	0.9 (± 0.09)	0.9 (± 0.11)		
Week 4 (n=22, 30)	0.9 (± 0.12)	0.9 (± 0.10)		
Week 8 (n=20, 26)	0.9 (± 0.10)	0.9 (± 0.09)		
Week 12 (n=15, 21)	1.0 (± 0.09)	0.9 (± 0.09)		
Week 16 (n=15, 19)	0.9 (± 0.11)	0.9 (± 0.10)		
Week 20 (n=7, 6)	0.9 (± 0.09)	0.9 (± 0.15)		
Week 24 (n=14, 17)	0.9 (± 0.10)	0.9 (± 0.10)		
Week 28 (n=7, 4)	1.0 (± 0.07)	1.0 (± 0.00)		
Week 32 (n=13, 13)	0.9 (± 0.10)	0.9 (± 0.12)		
Week 36 (n=6, 3)	0.9 (± 0.08)	1.0 (± 0.00)		
Week 40 (n=14, 13)	1.0 (± 0.08)	0.9 (± 0.18)		
Week 44 (n=7, 4)	1.0 (± 0.07)	1.0 (± 0.07)		
Week 48 (n=14, 12)	0.9 (± 0.11)	0.9 (± 0.11)		
Week 52 (n=13, 12)	0.9 (± 0.10)	0.9 (± 0.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D Y Index Scores in Subjects Between 8-17 Years of age: First Flare Free Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	43		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=38, 43)	0.9 (± 0.08)	0.9 (± 0.18)		
Week 4 (n=13, 28)	1.0 (± 0.06)	1.0 (± 0.07)		
Week 8 (n=9, 24)	1.0 (± 0.05)	1.0 (± 0.08)		
Week 12 (n=10, 25)	1.0 (± 0.07)	1.0 (± 0.06)		
Week 16 (n=7, 24)	1.0 (± 0.07)	1.0 (± 0.07)		
Week 20 (n=2, 11)	0.8 (± 0.01)	1.0 (± 0.05)		
Week 24 (n=6, 20)	1.0 (± 0.07)	1.0 (± 0.06)		
Week 28 (n=1, 9)	1.0 (± 99999)	1.0 (± 0.07)		
Week 32 (n=7, 19)	1.0 (± 0.07)	1.0 (± 0.07)		
Week 36 (n=0, 7)	99999 (± 99999)	1.0 (± 0.08)		
Week 40 (n=6, 17)	0.9 (± 0.09)	0.9 (± 0.14)		
Week 44 (n=0, 8)	99999 (± 99999)	0.9 (± 0.25)		
Week 48 (n=5, 16)	1.0 (± 0.08)	0.9 (± 0.09)		
Week 52 (n=4, 15)	1.0 (± 0.09)	1.0 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D Y Proxy Index Scores in Subjects Between 2-7 Years of age: First Flare Free Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of

problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	30		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 30)	1.0 (± 0.08)	0.9 (± 0.12)		
Week 4 (n=16, 14)	0.9 (± 0.10)	0.9 (± 0.14)		
Week 8 (n=11, 10)	1.0 (± 0.08)	1.0 (± 0.08)		
Week 12 (n=10, 10)	1.0 (± 0.09)	1.0 (± 0.06)		
Week 16 (n=7, 6)	0.9 (± 0.09)	1.0 (± 0.00)		
Week 20 (n=2, 3)	0.9 (± 0.12)	1.0 (± 0.00)		
Week 24 (n=4, 6)	0.9 (± 0.08)	1.0 (± 0.00)		
Week 28 (n=2, 3)	0.9 (± 0.12)	0.9 (± 0.09)		
Week 32 (n=4, 4)	0.9 (± 0.11)	1.0 (± 0.00)		
Week 36 (n=1, 3)	1.0 (± 99999)	1.0 (± 0.00)		
Week 40 (n=4, 3)	0.9 (± 0.11)	1.0 (± 0.00)		
Week 44 (n=1, 1)	1.0 (± 99999)	1.0 (± 99999)		
Week 48 (n=4, 3)	0.9 (± 0.11)	1.0 (± 0.00)		
Week 52 (n=5, 3)	1.0 (± 0.06)	1.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D-5L VAS Scores in Subjects >= 18 Years of age: First Flare Free Period

End point description:

EQ-5D-5L:subject rated questionnaire,6 questions to calculate health utility score. 2 components to EQ-5D-5L: 5-item health state profile assessed 5 dimensions:mobility,self-care,usual activities,pain/discomfort and anxiety/depression used to obtain Index Utility Score,VAS that measures health state. Each dimension:5 levels:1=no problems,2=slight,3=moderate,4=severe,5=extreme.Response to 5 dimensions comprised health state/a single utility index value.Eg. if subject responded"no problems"for each 5 dimensions, health state coded:"11111" with predefined index value to it.Every health state(coded as combination of responses on each of 5 dimensions):unique predefined utility index value assigned to it by EuroQol. US value sets(with all possible health states)used for adults in the study,range from 1 to -0.109. Higher(positive) scores= better health state. Eval-DB population analysed.'N':number of subjects

End point type	Secondary

End point timeframe:

Baseline(the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	48		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=46, 48)	88.3 (± 9.41)	85.2 (± 15.56)		
Week 4 (n=22, 30)	89.6 (± 9.11)	86.8 (± 10.74)		
Week 8 (n=20, 26)	91.3 (± 7.44)	88.5 (± 11.29)		
Week 12 (n=15, 21)	91.9 (± 8.86)	83.8 (± 15.36)		
Week 16 (n=15, 19)	91.3 (± 9.74)	86.1 (± 11.88)		
Week 20 (n=7, 6)	88.1 (± 12.01)	87.5 (± 14.01)		
Week 24 (n=14, 17)	92.6 (± 8.26)	88.1 (± 9.77)		
Week 28 (n=7, 4)	91.9 (± 7.06)	96.3 (± 2.75)		
Week 32 (n=13, 13)	91.5 (± 6.70)	89.5 (± 8.88)		
Week 36 (n=6, 3)	91.3 (± 9.83)	92.7 (± 10.12)		
Week 40 (n=14, 13)	93.1 (± 7.95)	87.2 (± 13.76)		
Week 44 (n=7, 4)	91.1 (± 9.63)	88.0 (± 11.78)		
Week 48 (n=14, 12)	92.5 (± 9.28)	92.4 (± 8.17)		
Week 52 (n=13, 12)	93.7 (± 7.75)	88.9 (± 9.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D Y VAS Scores in Subjects Between 8-17 Years of age: First Flare Free Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999:data not available.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	43		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=38, 43)	86.8 (± 14.86)	91.1 (± 9.34)		
Week 4 (n=13, 28)	87.7 (± 11.74)	91.6 (± 7.27)		
Week 8 (n=9, 24)	88.8 (± 10.96)	87.6 (± 14.84)		
Week 12 (n=10, 25)	89.8 (± 11.01)	87.9 (± 13.70)		
Week 16 (n=7, 24)	92.9 (± 8.01)	87.9 (± 14.74)		
Week 20 (n=2, 11)	84.0 (± 12.73)	86.1 (± 23.22)		
Week 24 (n=6, 20)	92.7 (± 12.04)	89.8 (± 13.76)		
Week 28 (n=1. 9)	96.0 (± 99999)	86.6 (± 15.40)		
Week 32 (n=7, 19)	92.1 (± 8.43)	88.8 (± 14.68)		
Week 36 (n=0, 7)	99999 (± 99999)	89.0 (± 18.25)		
Week 40 (n=6, 17)	95.2 (± 4.75)	89.6 (± 14.01)		
Week 44 (n=0, 8)	99999 (± 99999)	88.0 (± 16.46)		
Week 48 (n=5, 16)	93.8 (± 7.50)	89.1 (± 15.72)		
Week 52 (n=4, 15)	98.5 (± 1.91)	90.7 (± 13.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: First Flare Free Period

End point title	EuroQoL EQ-5D Y Proxy VAS Scores in Subjects Between 2-7 Years of age: First Flare Free Period

End point description:

EQ-5D-Y: child-friendly version of EQ-5D questionnaire related to health status. Health state profile assessed health in 5 dimensions (Mobility; Looking After Myself; Doing Usual Activities; Having Pain or Discomfort; Feeling Worried, Sad or Unhappy) used to obtain an index score, each of which had three levels of response (no problems/no pain/not worried, some problems/some pain/a bit worried, a lot of problems/a lot of pain/very worried). Scores ranged from <0 (where 0 is the value of a health state equivalent to dead; negative values: values as worse than dead) to 1 (the value of full health), higher scores=higher health utility. Proxy version was filled by care-giver of the subject. Eval-DB population was analysed. Here, 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points. 99999: data not available.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of OL period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	30		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=41, 30)	93.8 (± 9.97)	94.3 (± 8.16)		
Week 4 (n=16, 14)	94.6 (± 6.05)	96.3 (± 6.54)		
Week 8 (n=11, 10)	94.3 (± 7.06)	96.0 (± 7.29)		
Week 12 (n=10, 10)	94.4 (± 5.95)	98.3 (± 2.26)		
Week 16 (n=7, 6)	93.7 (± 8.22)	98.2 (± 2.23)		
Week 20 (n=2, 3)	96.5 (± 4.95)	93.7 (± 10.97)		
Week 24 (n=4, 6)	90.0 (± 8.49)	95.7 (± 5.01)		
Week 28 (n=2, 3)	100.0 (± 0.00)	100.0 (± 0.00)		
Week 32 (n=4, 4)	92.0 (± 8.45)	97.8 (± 1.71)		
Week 36 (n=1, 3)	100.0 (± 99999)	98.3 (± 2.89)		
Week 40 (n=4, 3)	91.5 (± 9.33)	99.3 (± 0.58)		
Week 44 (n=1, 1)	100.0 (± 99999)	100.0 (± 99999)		
Week 48 (4, 3)	94.0 (± 5.35)	99.0 (± 1.73)		
Week 52 (n=5, 3)	96.4 (± 4.16)	98.7 (± 2.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions were:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity). Percent work time missed due to health problem calculated as: Q2*100/(Q2+Q4) and score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-OL population analysed.'N':number of subjects evaluable for this end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=125)	5.75 (± 16.796)			
Week 2 (n=131)	4.72 (± 15.553)			
Week 4 (n=133)	5.92 (± 16.487)			
Week 6 (n=134)	4.83 (± 14.801)			
Week 8 (n=135)	6.96 (± 18.080)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity).Percent impairment while working due to health problem calculated as: 100*Q5/10 score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-OL population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific

End point type	Secondary

End point timeframe:

Weeks 0, 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=124)	32.66 (± 28.602)			
Week 2 (n=131)	17.02 (± 21.293)			
Week 4 (n=133)	15.26 (± 20.285)			

Week 6 (n=134)	14.10 (± 20.417)			
Week 8 (n=135)	14.37 (± 20.898)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity:regular daily activities(0-10 scale,high=less productivity).Percent overall impairment while working due to health problem calculated as:100*{Q2/(Q2+Q4)+[(1- Q2/(Q2+Q4))×(Q5/10)]},score ranged:0-100%,high numbers=greater impairment and less productivity.Eval-OL population analysed.'N':number of subjects evaluable for the end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	275			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=124)	34.77 (± 30.179)			
Week 2 (n=131)	20.10 (± 23.627)			
Week 4 (n=133)	19.30 (± 23.220)			
Week 6 (n=134)	17.43 (± 22.620)			
Week 8 (n=135)	19.36 (± 24.564)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent class time missed due to health problem calculated as: Q7*100/(Q7+Q8) and score ranged from 0-100% where higher numbers=greater impairment and less productivity. Eval-OL population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=83)	4.14 (± 14.982)			
Week 2 (n=98)	5.26 (± 16.664)			
Week 4 (n=108)	3.94 (± 12.968)			
Week 6 (n=117)	4.71 (± 13.991)			
Week 8 (n=118)	4.55 (± 14.584)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree

health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent impairment while in class was calculated as: 100*Q9/10 and score ranged from 0-100% where higher numbers indicate greater impairment and less productivity. Eval-OL population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=82)	26.46 (± 22.683)			
Week 2 (n=98)	17.55 (± 19.639)			
Week 4 (n=108)	15.37 (± 19.879)			
Week 6 (n=118)	13.31 (± 19.527)			
Week 8 (n=119)	12.69 (± 17.789)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent overall class impairment due to health problem calculated as: 100*{Q7/(Q7+Q8)+[(1- Q7/(Q7+Q8))×(Q9/10)]},score range:0-100%,higher numbers=greater impairment and less productivity.Eval-OL population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=82)	28.20 (± 24.171)			
Week 2 (n=98)	20.27 (± 22.676)			
Week 4 (n=108)	18.13 (± 22.977)			
Week 6 (n=117)	17.01 (± 23.126)			
Week 8 (n=118)	16.20 (± 22.148)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point title	Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: OL Run-in Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent activity impairment due to health problem calculated as: 100*Q10/10, score ranged from 0-100%,higher numbers=greater impairment and less productivity.Eval-OL population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	273			
Units: Units on a scale				
arithmetic mean (standard deviation)				

Baseline (n=268)	28.21 (± 28.766)			
Week 2 (n=271)	15.83 (± 20.036)			
Week 4 (n=273)	14.54 (± 20.162)			
Week 6 (n=273)	13.81 (± 20.547)			
Week 8 (n=273)	13.55 (± 19.783)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions were:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity). Percent work time missed due to health problem calculated as: Q2*100/(Q2+Q4) and score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	4.77 (± 14.528)	5.07 (± 14.128)		
Week 4 (n=11, 18)	5.67 (± 14.861)	5.54 (± 15.120)		
Week 8 (n=13, 17)	5.48 (± 14.237)	2.99 (± 12.345)		
Week 12 (n=13, 15)	3.98 (± 13.835)	3.85 (± 12.970)		
Week 16 (n=18, 21)	14.84 (± 30.656)	3.55 (± 10.903)		
Week 20 (n=8, 6)	4.34 (± 9.633)	0.37 (± 0.898)		

Week 24 (n=15, 18)	0.37 (± 0.997)	7.24 (± 17.750)		
Week 28 (n=5, 5)	0.36 (± 0.805)	0.82 (± 1.834)		
Week 32 (n=13, 18)	5.55 (± 14.500)	9.22 (± 25.636)		
Week 36 (n=5, 5)	5.00 (± 11.180)	0.84 (± 1.878)		
Week 40 (n=15, 18)	1.91 (± 6.181)	3.02 (± 11.770)		
Week 44 (n=6, 6)	0.27 (± 0.653)	0.70 (± 1.715)		
Week 48 (n=12, 15)	1.44 (± 3.746)	11.51 (± 21.033)		
Week 52 (n=15, 16)	11.27 (± 20.344)	5.00 (± 12.884)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=hours missed due to health problems;Q3=hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=hours missed due to health problems;Q8=hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity).Percent impairment while working due to health problem calculated as: 100*Q5/10 score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	9.71 (± 15.432)	10.26 (± 17.474)		
Week 4 (n=11, 18)	4.55 (± 12.136)	10.56 (± 15.136)		
Week 8 (n=13, 17)	6.15 (± 7.679)	5.29 (± 12.805)		

Week 12 (n=13, 15)	6.92 (± 8.549)	8.00 (± 20.771)		
Week 16 (n=17, 21)	11.76 (± 15.506)	5.24 (± 14.359)		
Week 20 (n=8, 6)	11.25 (± 15.526)	3.33 (± 5.164)		
Week 24 (n=15, 18)	8.00 (± 8.619)	8.89 (± 20.260)		
Week 28 (n=5, 5)	12.00 (± 13.038)	0.00 (± 0.000)		
Week 32 (n=13, 17)	7.69 (± 8.321)	9.41 (± 15.996)		
Week 36 (n=5, 5)	10.00 (± 10.000)	10.00 (± 10.000)		
Week 40 (n=15, 18)	9.33 (± 10.998)	10.56 (± 19.844)		
Week 44 (n=6, 6)	21.67 (± 32.506)	11.67 (± 24.014)		
Week 48 (n=12, 15)	9.17 (± 9.003)	13.33 (± 21.269)		
Week 52 (n=15, 16)	8.00 (± 9.411)	10.63 (± 20.484)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity:regular daily activities(0-10 scale,high=less productivity).Percent overall impairment while working due to health problem calculated as:100*{Q2/(Q2+Q4)+[(1- Q2/(Q2+Q4))×(Q5/10)]},score ranged:0-100%,high numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for the end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	14.04 (± 19.991)	14.29 (± 21.183)		
Week 4 (n=11, 18)	10.20 (± 17.730)	15.53 (± 20.088)		
Week 8 (n=13, 17)	11.46 (± 14.980)	8.29 (± 16.813)		
Week 12 (n=13, 15)	10.11 (± 16.906)	9.13 (± 23.216)		
Week 16 (n=17, 21)	21.06 (± 24.410)	7.17 (± 19.121)		
Week 20 (n=8, 6)	15.15 (± 17.456)	3.67 (± 5.715)		
Week 24 (n=15, 18)	8.33 (± 8.906)	15.35 (± 25.202)		
Week 28 (n=5, 5)	12.32 (± 12.997)	0.82 (± 1.834)		
Week 32 (n=13, 17)	12.69 (± 16.267)	11.35 (± 20.568)		
Week 36 (n=5, 5)	14.50 (± 14.186)	10.76 (± 10.143)		
Week 40 (n=15, 18)	11.01 (± 12.629)	11.33 (± 21.941)		
Week 44 (n=6, 6)	21.93 (± 32.299)	12.37 (± 23.664)		
Week 48 (n=12, 15)	10.36 (± 10.518)	20.64 (± 28.599)		
Week 52 (n=15, 16)	17.91 (± 21.428)	14.68 (± 23.128)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent class time missed due to health problem calculated as: Q7*100/(Q7+Q8) and score ranged from 0-100% where higher numbers=greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period),Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	0.04 (± 0.223)	2.22 (± 9.030)		
Week 4 (n=12, 22)	0.89 (± 3.089)	1.14 (± 5.330)		
Week 8 (n=12, 19)	0.00 (± 0.000)	1.62 (± 6.735)		
Week 12 (n=8, 18)	11.36 (± 32.138)	3.09 (± 11.781)		
Week 16 (n=9, 14)	0.00 (± 0.000)	7.64 (± 23.561)		
Week 20 (n=7, 9)	7.79 (± 20.599)	0.00 (± 0.000)		
Week 24 (n=8, 20)	0.00 (± 0.000)	3.62 (± 9.881)		
Week 28 (n=5, 7)	0.00 (± 0.000)	0.00 (± 0.000)		
Week 32 (n=8, 20)	0.00 (± 0.000)	5.83 (± 15.897)		
Week 36 (n=4, 4)	0.00 (± 0.000)	0.00 (± 0.000)		
Week 40 (n=5, 14)	0.00 (± 0.000)	3.57 (± 13.363)		
Week 44 (n=5, 6)	0.00 (± 0.000)	0.00 (± 0.000)		
Week 48 (n=9, 17)	11.11 (± 33.333)	0.00 (± 0.000)		
Week 52 (n=7, 22)	5.71 (± 15.119)	9.09 (± 25.054)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent impairment while in class was calculated as: 100*Q9/10 and score ranged from 0-100% where higher numbers indicate greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	8.62 (± 14.072)	7.88 (± 11.390)		
Week 4 (n=12, 22)	5.83 (± 12.401)	6.36 (± 12.168)		
Week 8 (n=12, 19)	4.17 (± 7.930)	5.79 (± 8.377)		
Week 12 (n=8, 18)	3.75 (± 7.440)	2.22 (± 7.321)		
Week 16 (n=9, 14)	7.78 (± 16.415)	8.57 (± 10.271)		
Week 20 (n=7, 9)	11.43 (± 16.762)	11.11 (± 26.667)		
Week 24 (n=8, 20)	8.75 (± 18.077)	4.00 (± 7.539)		
Week 28 (n=5, 7)	10.00 (± 22.361)	7.14 (± 11.127)		
Week 32 (n=8, 20)	3.75 (± 10.607)	3.50 (± 9.333)		
Week 36 (n=4, 4)	2.50 (± 5.000)	2.50 (± 5.000)		
Week 40 (n=5, 14)	2.00 (± 4.472)	8.57 (± 14.064)		
Week 44 (n=5, 6)	10.00 (± 14.142)	6.67 (± 8.165)		
Week 48 (n=8, 17)	7.50 (± 13.887)	7.06 (± 12.127)		
Week 52 (n=7, 21)	1.43 (± 3.780)	7.62 (± 14.458)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);

Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent overall class impairment due to health problem calculated as: 100*{Q7/(Q7+Q8)+[(1- Q7/(Q7+Q8))×(Q9/10)]},score range:0-100%,higher numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	8.64 (± 14.136)	10.10 (± 13.237)		
Week 4 (n=12, 22)	6.37 (± 14.034)	7.50 (± 12.701)		
Week 8 (n=12, 19)	4.17 (± 7.930)	7.40 (± 9.858)		
Week 12 (n=8, 18)	15.11 (± 31.477)	5.28 (± 13.559)		
Week 16 (n=9, 14)	7.78 (± 16.415)	14.06 (± 24.697)		
Week 20 (n=7, 9)	18.44 (± 24.535)	11.11 (± 26.667)		
Week 24 (n=8, 20)	8.75 (± 18.077)	7.20 (± 13.260)		
Week 28 (n=5, 7)	10.00 (± 22.361)	7.14 (± 11.127)		
Week 32 (n=8, 20)	3.75 (± 10.607)	9.06 (± 18.186)		
Week 36 (n=4, 4)	2.50 (± 5.000)	2.50 (± 5.000)		
Week 40 (n=5, 14)	2.00 (± 4.472)	11.79 (± 18.771)		
Week 44 (n=5, 6)	10.00 (± 14.142)	6.67 (± 8.165)		
Week 48 (n=8, 17)	7.50 (± 13.887)	7.06 (± 12.127)		
Week 52 (n=7, 21)	7.14 (± 14.960)	11.90 (± 20.154)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point title	Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: DB Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent activity impairment due to health problem calculated as: 100*Q10/10, score ranged from 0-100%,higher numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=69, 78)	8.99 (± 15.353)	10.90 (± 16.763)		
Week 4 (n=32, 51)	10.31 (± 18.749)	8.24 (± 13.222)		
Week 8 (n=36, 50)	8.61 (± 13.555)	7.20 (± 12.784)		
Week 12 (n=32, 49)	10.31 (± 16.749)	5.31 (± 13.087)		
Week 16 (n=42, 52)	10.00 (± 15.927)	7.12 (± 14.731)		
Week 20 (n=21, 21)	16.19 (± 22.017)	9.52 (± 21.089)		
Week 24 (n=37, 47)	8.38 (± 13.645)	5.74 (± 12.810)		
Week 28 (n=18, 17)	11.67 (± 16.891)	5.29 (± 12.805)		
Week 32 (n=34, 45)	9.12 (± 17.815)	6.89 (± 14.744)		
Week 36 (n=17, 17)	11.18 (± 15.363)	9.41 (± 13.449)		
Week 40 (n=34, 47)	10.59 (± 18.081)	8.30 (± 17.235)		
Week 44 (n=18, 17)	13.33 (± 21.693)	7.65 (± 16.781)		
Week 48 (n=30, 43)	11.00 (± 16.263)	6.05 (± 13.997)		
Week 52 (n=32, 43)	7.50 (± 14.368)	7.21 (± 15.480)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions were:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity). Percent work time missed due to health problem calculated as: Q2*100/(Q2+Q4) and score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	4.77 (± 14.528)	5.07 (± 14.128)		
Week 4 (n=10, 18)	5.76 (± 15.662)	5.54 (± 15.120)		
Week 8 (n=9, 14)	7.50 (± 16.965)	3.64 (± 13.604)		
Week 12 (n=7, 10)	7.14 (± 18.898)	5.77 (± 15.790)		
Week 16 (n=7, 14)	23.49 (± 38.319)	5.32 (± 13.142)		
Week 20 (n=2, 3)	0.00 (± 0.000)	0.73 (± 1.270)		
Week 24 (n=7, 10)	0.34 (± 0.907)	8.03 (± 18.722)		
Week 28 (n=2, 2)	0.00 (± 0.000)	2.05 (± 2.899)		
Week 32 (n=6, 11)	11.75 (± 20.454)	15.08 (± 31.936)		
Week 36 (n=2, 3)	0.00 (± 0.000)	1.40 (± 2.425)		
Week 40 (n=7, 11)	0.69 (± 1.814)	4.95 (± 15.001)		
Week 44 (n=3, 3)	0.00 (± 0.000)	1.40 (± 2.425)		
Week 48 (n=7, 10)	1.79 (± 4.725)	12.27 (± 21.541)		
Week 52 (n=6, 9)	8.33 (± 20.412)	3.33 (± 6.022)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=hours missed due to health problems;Q3=hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=hours missed due to health problems;Q8=hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity).Percent impairment while working due to health problem calculated as: 100*Q5/10 score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	9.71 (± 15.432)	10.26 (± 17.474)		
Week 4 (n=10, 18)	5.00 (± 12.693)	10.56 (± 15.136)		
Week 8 (n=9, 14)	4.44 (± 5.270)	6.43 (± 13.927)		
Week 12 (n=7, 10)	5.71 (± 7.868)	12.00 (± 24.855)		
Week 16 (n=6, 14)	8.33 (± 11.690)	7.86 (± 17.177)		
Week 20 (n=2, 3)	15.00 (± 21.213)	6.67 (± 5.774)		
Week 24 (n=7, 10)	8.57 (± 8.997)	13.00 (± 25.408)		
Week 28 (n=2, 2)	10.00 (± 14.142)	0.00 (± 0.000)		

Week 32 (n=6, 10)	8.33 (± 7.528)	15.00 (± 19.003)		
Week 36 (n=2, 3)	10.00 (± 14.142)	10.00 (± 10.000)		
Week 40 (n=7, 11)	12.86 (± 11.127)	14.55 (± 23.394)		
Week 44 (n=3, 3)	30.00 (± 43.589)	23.33 (± 32.146)		
Week 48 (n=7, 10)	11.43 (± 8.997)	16.00 (± 24.585)		
Week 52 (n=6, 9)	8.33 (± 7.528)	15.56 (± 25.055)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity:regular daily activities(0-10 scale,high=less productivity).Percent overall impairment while working due to health problem calculated as:100*{Q2/(Q2+Q4)+[(1- Q2/(Q2+Q4))×(Q5/10)]},score ranged:0-100%,high numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for the end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	38		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=35, 38)	14.04 (± 19.991)	14.29 (± 21.183)		
Week 4 (n=10, 18)	10.74 (± 18.593)	15.53 (± 20.088)		
Week 8 (n=9, 14)	11.77 (± 16.662)	10.06 (± 18.129)		
Week 12 (n=7, 10)	11.43 (± 21.931)	13.70 (± 27.729)		

Week 16 (n=6, 14)	17.57 (± 23.791)	10.75 (± 22.825)		
Week 20 (n=2, 3)	15.00 (± 21.213)	7.33 (± 6.429)		
Week 24 (n=7, 10)	8.86 (± 9.442)	19.63 (± 29.412)		
Week 28 (n=2, 2)	10.00 (± 14.142)	2.05 (± 2.899)		
Week 32 (n=6, 10)	18.92 (± 20.929)	18.29 (± 24.749)		
Week 36 (n=2, 3)	10.00 (± 14.142)	11.27 (± 10.238)		
Week 40 (n=7, 11)	13.40 (± 11.616)	15.82 (± 26.160)		
Week 44 (n=3, 3)	30.00 (± 43.589)	24.73 (± 30.679)		
Week 48 (n=7, 10)	12.86 (± 11.127)	23.46 (± 29.836)		
Week 52 (n=6, 9)	15.83 (± 20.595)	17.20 (± 25.996)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent class time missed due to health problem calculated as: Q7*100/(Q7+Q8) and score ranged from 0-100% where higher numbers=greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	0.04 (± 0.223)	2.22 (± 9.030)		
Week 4 (n=11, 22)	0.97 (± 3.226)	1.14 (± 5.330)		
Week 8 (n=7, 19)	0.00 (± 0.000)	1.62 (± 6.735)		
Week 12 (n=4, 17)	0.00 (± 0.000)	3.27 (± 12.118)		
Week 16 (n=4, 13)	0.00 (± 0.000)	8.22 (± 24.416)		
Week 20 (n=1, 7)	0.00 (± 99999)	0.00 (± 0.000)		
Week 24 (n=2, 14)	0.00 (± 0.000)	0.71 (± 2.673)		
Week 28 (n=0, 4)	99999 (± 99999)	0.00 (± 0.000)		
Week 32 (n=2, 13)	0.00 (± 0.000)	8.97 (± 19.226)		
Week 36 (n=0, 2)	99999 (± 99999)	0.00 (± 0.000)		
Week 40 (n=2, 8)	0.00 (± 0.000)	0.00 (± 0.000)		
Week 44 (n=1, 3)	0.00 (± 99999)	0.00 (± 0.000)		
Week 48 (n=4, 9)	0.00 (± 0.000)	0.00 (± 0.000)		
Week 52 (n=2, 9)	0.00 (± 0.000)	0.00 (± 0.000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent impairment while in class was calculated as: 100*Q9/10 and score ranged from 0-100% where higher numbers indicate greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	8.62 (± 14.072)	7.88 (± 11.390)		
Week 4 (n=11, 22)	6.36 (± 12.863)	6.36 (± 12.168)		
Week 8 (n=7, 19)	1.43 (± 3.780)	5.79 (± 8.377)		
Week 12 (n=4, 17)	5.00 (± 10.000)	2.35 (± 7.524)		
Week 16 (n=4, 13)	2.50 (± 5.000)	8.46 (± 10.682)		
Week 20 (n=1, 7)	0.00 (± 99999)	14.29 (± 29.921)		
Week 24 (n=2, 14)	10.00 (± 14.142)	2.86 (± 6.112)		
Week 28 (n=0, 4)	99999 (± 99999)	10.00 (± 14.142)		
Week 32 (n=2, 13)	0.00 (± 0.000)	3.85 (± 11.209)		
Week 36 (n=0, 2)	99999 (± 99999)	5.00 (± 7.071)		
Week 40 (n=2, 8)	5.00 (± 7.071)	6.25 (± 9.161)		
Week 44 (n=1, 3)	20.00 (± 99999)	10.00 (± 10.000)		
Week 48 (n=4, 9)	7.50 (± 15.000)	5.56 (± 11.304)		
Week 52 (n=2, 9)	0.00 (± 0.000)	3.33 (± 7.071)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent overall class impairment due to health problem calculated as: 100*{Q7/(Q7+Q8)+[(1- Q7/(Q7+Q8))×(Q9/10)]},score range:0-100%,higher numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for this

evaluable at specific time points.

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	33		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=29, 33)	8.64 (± 14.136)	10.10 (± 13.237)		
Week 4 (n=11, 22)	6.95 (± 14.568)	7.50 (± 12.701)		
Week 8 (n=7, 19)	1.43 (± 3.780)	7.40 (± 9.858)		
Week 12 (n=4, 17)	5.00 (± 10.000)	5.59 (± 13.910)		
Week 16 (n=4, 13)	2.50 (± 5.000)	14.37 (± 25.677)		
Week 20 (n=1, 7)	0.00 (± 99999)	14.29 (± 29.921)		
Week 24 (n=2, 14)	10.00 (± 14.142)	3.50 (± 7.283)		
Week 28 (n=0, 4)	99999 (± 99999)	0.00 (± 8.165)		
Week 32 (n=2, 13)	0.00 (± 0.000)	12.39 (± 21.847)		
Week 36 (n=0, 2)	99999 (± 99999)	5.00 (± 7.071)		
Week 40 (n=2, 8)	5.00 (± 7.071)	6.25 (± 9.161)		
Week 44 (n=1, 3)	20.00 (± 99999)	10.00 (± 10.000)		
Week 48 (n=4, 9)	7.50 (± 15.000)	5.56 (± 11.304)		
Week 52 (n= 2, 9)	0.00 (± 0.000)	3.33 (± 7.071)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point title	Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Free Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5=degree

health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent activity impairment due to health problem calculated as: 100*Q10/10, score ranged from 0-100%,higher numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific

End point type	Secondary

End point timeframe:

Baseline (the last observation up to and including Day 1 of DB period), Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	78		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=69, 78)	8.99 (± 15.353)	10.90 (± 16.763)		
Week 4 (n=30, 51)	11.00 (± 19.182)	8.24 (± 13.222)		
Week 8 (n=25, 44)	10.00 (± 15.275)	7.27 (± 13.005)		
Week 12 (n=20, 40)	10.50 (± 18.202)	5.50 (± 13.765)		
Week 16 (n=19, 37)	8.95 (± 15.949)	8.11 (± 15.958)		
Week 20 (n=8, 13)	15.00 (± 16.903)	9.23 (± 22.159)		
Week 24 (n=17, 31)	8.24 (± 13.339)	5.81 (± 13.850)		
Week 28 (n=7, 9)	17.14 (± 17.995)	3.33 (± 7.071)		
Week 32 (n=16, 27)	11.88 (± 22.574)	8.52 (± 17.255)		
Week 36 (n=6, 7)	15.00 (± 13.784)	8.57 (± 8.997)		
Week 40 (n=17, 26)	12.35 (± 17.864)	7.31 (± 16.385)		
Week 44 (n=7, 9)	15.71 (± 17.182)	8.89 (± 16.915)		
Week 48 (n=17, 24)	11.18 (± 16.539)	7.50 (± 16.485)		
Week 52 (n=15, 23)	12.00 (± 17.403)	6.52 (± 16.951)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Work Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions were:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity). Percent work time missed due to health problem calculated as: Q2*100/(Q2+Q4) and score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point, 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=19, 15)	5.46 (± 14.226)	6.99 (± 18.460)		
Week 4 (n=10, 5)	1.49 (± 3.188)	0.00 (± 0.000)		
Week 8 (n=5, 2)	2.36 (± 5.277)	0.00 (± 0.000)		
Week 12 (n=2, 1)	34.40 (± 48.649)	0.00 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Impairment While Working Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=hours missed due to health problems;Q3=hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=hours missed due to health problems;Q8=hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale,high=less productivity).Percent impairment while working due to health problem calculated as: 100*Q5/10 score ranged from 0-100%,higher numbers=greater impairment and less productivity. Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=19, 15)	11.05 (± 14.868)	16.67 (± 31.547)		
Week 4 (n=10, 5)	12.00 (± 18.738)	10.00 (± 10.000)		
Week 8 (n=5, 2)	8.00 (± 17.889)	15.00 (± 21.213)		
Week 12 (n=2, 1)	50.00 (± 14.142)	0.00 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Overall Work Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity:regular daily activities(0-10 scale,high=less productivity).Percent overall impairment while working due to health problem calculated as:100*{Q2/(Q2+Q4)+[(1- Q2/(Q2+Q4))×(Q5/10)]},score ranged:0-100%,high numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for the end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=19, 15)	16.21 (± 18.311)	20.32 (± 32.634)		
Week 4 (n=10, 5)	13.40 (± 18.431)	10.00 (± 10.000)		
Week 8 (n=5, 2)	10.36 (± 17.339)	15.00 (± 21.213)		
Week 12 (n=2, 1)	70.65 (± 15.061)	0.00 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Class Time Missed Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working(0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent class time missed due to health problem calculated as: Q7*100/(Q7+Q8) and score ranged from 0-100% where higher numbers=greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	16		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=13, 16)	3.98 (± 12.314)	11.53 (± 27.668)		
Week 4 (n=6, 12)	0.00 (± 0.000)	6.82 (± 16.215)		
Week 8 (n=2, 6)	0.00 (± 0.000)	8.33 (± 20.412)		

Week 12 (n=0, 4)	99999 (± 99999)	1.43 (± 2.850)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Impairment While in Class Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days. Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5 = degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale, high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent impairment while in class was calculated as: 100*Q9/10 and score ranged from 0-100% where higher numbers indicate greater impairment and less productivity. Eval-DB population analysed. 'N': number of subjects evaluable for this end point and 'n': number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=13, 15)	13.85 (± 17.578)	24.67 (± 28.999)		
Week 4 (n=6, 12)	16.67 (± 13.663)	25.00 (± 25.761)		
Week 8 (n=2, 6)	30.00 (± 14.142)	30.00 (± 26.077)		
Week 12 (n=0, 4)	99999 (± 99999)	40.00 (± 28.284)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Overall Class Impairment Using Work Productivity and Activity

Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Overall Class Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire to assess degree to which AD affected work productivity and regular activities over past7days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked;Q5=degree health affected productivity while working (0-10 scale,high=less productivity);Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity).Percent overall class impairment due to health problem calculated as: 100*{Q7/(Q7+Q8)+[(1- Q7/(Q7+Q8))×(Q9/10)]},score range:0-100%,higher numbers=greater impairment and less productivity.Eval-DB population analysed.'N':number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	15		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=13, 15)	17.49 (± 19.742)	25.60 (± 30.354)		
Week 4 (n=6, 12)	16.67 (± 13.663)	30.21 (± 26.983)		
Week 8 (n=2, 6)	30.00 (± 14.142)	34.17 (± 31.371)		
Week 12 (n=0, 4)	99999 (± 99999)	40.28 (± 28.803)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point title	Percent Activity Impairment Using Work Productivity and Activity Impairment Questionnaire Plus Classroom Impairment Questions: First Flare Period

End point description:

WPAI+CIQ:10-item questionnaire used to assess degree to which AD affected work productivity and regular activities over past 7 days.Questions:Q1=currently employed;Q2=work hours missed due to health problems;Q3=work hours missed due to other reasons;Q4=hours actually worked; Q5=degree health affected productivity while working (0-10 scale, high=less productivity); Q6=classes attended in academic setting or not;Q7=class hours missed due to health problems;Q8=class hours actually attended;Q9=degree health affected productivity while attending(0-10 scale,high= productivity);Q10=degree health affected productivity in regular daily activities(0-10 scale, high=less productivity). Percent activity impairment due to health problem calculated as: 100*Q10/10, scores ranged from 0-100%,higher numbers=greater impairment and less productivity.Eval-DB population

number of subjects evaluable for this end point,'n':number of subjects evaluable at specific time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	44		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 0 (n=43, 44)	14.88 (± 20.745)	17.27 (± 23.164)		
Week 4 (n=21, 24)	15.24 (± 20.401)	19.17 (± 21.653)		
Week 8 (n=13, 15)	13.85 (± 17.578)	26.00 (± 28.486)		
Week 12 (n=3, 7)	16.67 (± 20.817)	31.43 (± 29.681)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: OL Run-in Period

End point title	Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: OL Run-in Period

End point description:

HADS was a validated 14-item questionnaire to assess states of anxiety and depression over the past week. HADS consisted of 2 subscales: HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D), each of which comprised of 7 items. Each item was rated on a 4-point scale, with scores ranging from 0 to 3, where higher scores indicated more anxiety/depression symptoms. HADS-A assessed state of generalized anxiety. HADS-A total score =sum of all 7 items with score ranging from 0 (no presence of anxiety) to 21 (severe feeling of anxiety); higher score indicated greater severity of anxiety. HADS-D assessed the state of lost interest and diminished pleasure response. HADS-D total score =the sum of all 7 items with score ranging from 0 (no presence of depression) to 21 (severe feeling of depression); higher score indicated greater severity of depression symptoms. Evaluable OL population was analysed. Here, 'N: 'number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6 and 8

End point values	Crisaborole 2% BID			
Subject group type	Reporting group			
Number of subjects analysed	270			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Anxiety: Baseline	5.3 (± 3.70)			
Anxiety: Week 2	5.3 (± 3.73)			
Anxiety: Week 4	5.3 (± 3.72)			
Anxiety: Week 6	5.4 (± 3.79)			
Anxiety: Week 8	5.4 (± 3.81)			
Depression: Baseline	3.2 (± 3.09)			
Depression: Week 2	3.2 (± 3.09)			
Depression: Week 4	3.2 (± 3.11)			
Depression: Week 6	3.3 (± 3.16)			
Depression: Week 8	3.3 (± 3.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: DB Period

End point title	Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: DB Period

End point description:

HADS: validated 14-item questionnaire to assess states of anxiety and depression over the past week. HADS consisted of 2 subscales: HADS-A and HADS-D, each of which comprised of 7 items. Each item was rated on a 4-point scale, with scores ranging from 0 to 3, where higher scores indicated more anxiety/depression symptoms. HADS-A assessed state of generalized anxiety. HADS-A total score =sum of all 7 items with score ranging from 0 (no presence of anxiety) to 21 (severe feeling of anxiety); higher score indicated greater severity of anxiety. HADS-D assessed the state of lost interest and diminished pleasure response. HADS-D total score =the sum of all 7 items with score ranging from 0 (no presence of depression) to 21 (severe feeling of depression); higher score indicated greater severity of depression symptoms. Evaluable DB population was analysed. Here, 'N': number of subjects evaluable for this end point and n: subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 8, 16, 32 and end of treatment (Week 52)

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	77		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Anxiety: Baseline (n=66,77)	4.5 (± 3.50)	4.5 (± 3.59)		
Anxiety: Week 8 (n=31, 50)	3.6 (± 3.23)	4.5 (± 3.09)		
Anxiety: Week 16 (n=38, 48)	4.6 (± 3.83)	4.7 (± 3.58)		
Anxiety: Week 32 (n=35, 47)	3.3 (± 3.42)	4.4 (± 4.00)		

Anxiety: End of treatment (n=35, 49)	4.0 (± 3.95)	4.7 (± 3.62)		
Depression: Baseline (n=66, 77)	2.7 (± 2.36)	2.8 (± 2.94)		
Depression: Week 8 (n=31, 50)	2.1 (± 2.00)	2.5 (± 2.65)		
Depression: Week 16 (n=38, 48)	2.9 (± 2.65)	3.5 (± 3.76)		
Depression: Week 32 (n=35, 47)	2.6 (± 2.82)	3.3 (± 3.76)		
Depression: End of treatment (n=35, 49)	2.8 (± 2.77)	3.4 (± 3.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: First Flare Period

End point title	Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: First Flare Period

End point description:

HADS: validated 14-item questionnaire to assess states of anxiety and depression over the past week. HADS consisted of 2 subscales: HADS-A and HADS-D, each of which comprised of 7 items. Each item was rated on a 4-point scale, with scores ranging from 0 to 3, where higher scores indicated more anxiety/depression symptoms. HADS-A assessed state of generalized anxiety. HADS-A total score =sum of all 7 items with score ranging from 0 (no presence of anxiety) to 21 (severe feeling of anxiety); higher score indicated greater severity of anxiety. HADS-D assessed the state of lost interest and diminished pleasure response. HADS-D total score =the sum of all 7 items with score ranging from 0 (no presence of depression) to 21 (severe feeling of depression); higher score indicated greater severity of depression symptoms. Evaluable DB population was analysed. Here, 'N': number of subjects evaluable for this end point and n: subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Weeks 0, 4, 8 and 12

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	18		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Anxiety: Week 0 (n=11, 14)	3.7 (± 3.52)	4.9 (± 3.70)		
Anxiety: Week 4 (n=15, 18)	4.3 (± 3.46)	5.8 (± 4.19)		
Anxiety: Week 8 (n=4, 5)	4.3 (± 1.89)	8.0 (± 5.24)		
Anxiety: Week 12 (n=3, 6)	6.0 (± 1.00)	5.0 (± 4.73)		
Depression: Week 0 (n=11, 14)	2.4 (± 3.07)	2.5 (± 3.16)		
Depression: Week 4 (n=15, 18)	3.1 (± 2.79)	4.2 (± 5.19)		
Depression: Week 8 (n=4, 5)	1.3 (± 1.26)	4.8 (± 4.44)		
Depression: Week 12 (n=3, 6)	1.0 (± 1.00)	3.3 (± 2.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: First Flare Free Period

End point title	Total Anxiety and Depression Scores Measured Using Hospital Anxiety and Depression Scale: First Flare Free Period

End point description:

HADS: validated 14-item questionnaire to assess states of anxiety and depression over the past week. HADS consisted of 2 subscales: HADS-A and HADS-D, each of which comprised of 7 items. Each item was rated on a 4-point scale, with scores ranging from 0 to 3, where higher scores indicated more anxiety/depression symptoms. HADS-A assessed state of generalized anxiety. HADS-A total score =sum of all 7 items with score ranging from 0 (no presence of anxiety) to 21 (severe feeling of anxiety); higher score indicated greater severity of anxiety. HADS-D assessed the state of lost interest and diminished pleasure response. HADS-D total score =the sum of all 7 items with score ranging from 0 (no presence of depression) to 21 (severe feeling of depression); higher score indicated greater severity of depression symptoms. Evaluable DB population was analysed. Here, 'N': number of subjects evaluable for this end point and n: subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Baseline (last observation up to and including the randomisation day), Weeks 8, 16 and 32

End point values	Vehicle QD	Crisaborole 2% QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	77		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Anxiety: Baseline (n=66, 77)	4.5 (± 3.50)	4.5 (± 3.59)		
Anxiety: Week 8 (n=25, 44)	3.8 (± 3.28)	4.1 (± 2.74)		
Anxiety: Week 16 (n=19, 38)	3.9 (± 3.38)	4.3 (± 3.49)		
Anxiety: Week 32 (n=17, 28)	2.9 (± 2.47)	4.2 (± 3.79)		
Depression: Baseline (n=66, 77)	2.7 (± 2.36)	2.8 (± 2.94)		
Depression: Week 8 (n=25, 44)	2.2 (± 2.13)	2.2 (± 2.29)		
Depression: Week 16 (n=19, 38)	2.1 (± 1.91)	3.1 (± 3.46)		
Depression: Week 32 (n=17, 28)	1.9 (± 2.22)	3.0 (± 3.00)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study intervention up to 8 weeks of OL period (OL: Crisaborole 2% BID arm); From start of study intervention in DB period to 28 days after last dose of study intervention (Up to 56 weeks) for DB: vehicle QD and DB: Crisaborole 2% QD arms

Adverse event reporting additional description:

Same event may appear as both AE and SAE, but are distinct events. An event may be categorized as serious in 1 subject and non-serious in another, or a subject may have experienced both AE and non-SAE. Safety population comprised of all subjects who received at least 1 dose of study intervention during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v24.1

Reporting groups

Reporting group title	OL: Crisaborole 2% BID

Reporting group description:

Subjects with mild to moderate AD were administered Crisaborole 2% BID in OL period for maximum duration of up to 8 weeks. The subjects that responded during this period were randomized to DB in a 1:1 ratio and received Crisaborole 2% QD or vehicle for 52 weeks.

Reporting group title	DB: Vehicle

Reporting group description:

The subjects that responded during the OL period were randomized to DB period in a 1:1 ratio and received vehicle QD for 52 weeks.

Reporting group title	DB: Crisaborole 2% QD

Reporting group description:

The subjects that responded during the OL period were randomized to DB period in a 1:1 ratio and received Crisaborole 2% QD for 52 weeks.

Serious adverse events	OL: Crisaborole 2% BID	DB: Vehicle	DB: Crisaborole 2% QD
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 497 (0.60%)	4 / 135 (2.96%)	3 / 135 (2.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Foreign body ingestion			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Maternal exposure during pregnancy			

subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paternal exposure during pregnancy			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Application site infection			

subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	OL: Crisaborole 2% BID	DB: Vehicle	DB: Crisaborole 2% QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 497 (14.89%)	41 / 135 (30.37%)	32 / 135 (23.70%)
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 497 (0.20%)	0 / 135 (0.00%)	3 / 135 (2.22%)
occurrences (all)	1	0	4
Skin laceration			
subjects affected / exposed	1 / 497 (0.20%)	1 / 135 (0.74%)	2 / 135 (1.48%)
occurrences (all)	1	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	3 / 135 (2.22%)
occurrences (all)	0	1	3
General disorders and administration site conditions			

Application site erythema			
subjects affected / exposed	5 / 497 (1.01%)	1 / 135 (0.74%)	0 / 135 (0.00%)
occurrences (all)	6	1	0
Application site pain			
subjects affected / exposed	28 / 497 (5.63%)	3 / 135 (2.22%)	1 / 135 (0.74%)
occurrences (all)	44	3	1
Pyrexia			
subjects affected / exposed	1 / 497 (0.20%)	3 / 135 (2.22%)	1 / 135 (0.74%)
occurrences (all)	1	3	1
Application site pruritus			
subjects affected / exposed	5 / 497 (1.01%)	1 / 135 (0.74%)	0 / 135 (0.00%)
occurrences (all)	5	1	0
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 497 (0.20%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 497 (0.20%)	3 / 135 (2.22%)	0 / 135 (0.00%)
occurrences (all)	1	3	0
Constipation			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	1 / 497 (0.20%)	2 / 135 (1.48%)	1 / 135 (0.74%)
occurrences (all)	2	2	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	1 / 497 (0.20%)	3 / 135 (2.22%)	0 / 135 (0.00%)
occurrences (all)	1	3	0
Nasal congestion			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	2 / 135 (1.48%)
occurrences (all)	0	2	3

Oropharyngeal pain			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	3 / 135 (2.22%)
occurrences (all)	0	1	5
Rhinitis allergic			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	1 / 135 (0.74%)
occurrences (all)	0	2	1
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	12 / 497 (2.41%)	5 / 135 (3.70%)	2 / 135 (1.48%)
occurrences (all)	13	5	2
Dermatitis contact			
subjects affected / exposed	4 / 497 (0.80%)	4 / 135 (2.96%)	1 / 135 (0.74%)
occurrences (all)	4	5	1
Eczema			
subjects affected / exposed	4 / 497 (0.80%)	2 / 135 (1.48%)	1 / 135 (0.74%)
occurrences (all)	4	2	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	2 / 135 (1.48%)
occurrences (all)	0	0	2
Sleep disorder			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	2 / 135 (1.48%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 497 (0.20%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	2 / 135 (1.48%)
occurrences (all)	0	1	2
Infections and infestations			
Application site infection			
subjects affected / exposed	6 / 497 (1.21%)	5 / 135 (3.70%)	2 / 135 (1.48%)
occurrences (all)	6	7	2
Bronchitis			

subjects affected / exposed	2 / 497 (0.40%)	3 / 135 (2.22%)	0 / 135 (0.00%)
occurrences (all)	2	3	0
COVID-19			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	6 / 135 (4.44%)
occurrences (all)	0	1	6
Conjunctivitis			
subjects affected / exposed	1 / 497 (0.20%)	2 / 135 (1.48%)	0 / 135 (0.00%)
occurrences (all)	1	2	0
Folliculitis			
subjects affected / exposed	0 / 497 (0.00%)	3 / 135 (2.22%)	1 / 135 (0.74%)
occurrences (all)	0	3	1
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 497 (0.00%)	1 / 135 (0.74%)	2 / 135 (1.48%)
occurrences (all)	0	1	2
Influenza			
subjects affected / exposed	4 / 497 (0.80%)	1 / 135 (0.74%)	3 / 135 (2.22%)
occurrences (all)	4	1	4
Nasopharyngitis			
subjects affected / exposed	4 / 497 (0.80%)	5 / 135 (3.70%)	1 / 135 (0.74%)
occurrences (all)	4	5	1
Otitis media			
subjects affected / exposed	1 / 497 (0.20%)	1 / 135 (0.74%)	2 / 135 (1.48%)
occurrences (all)	1	1	4
Oral herpes			
subjects affected / exposed	0 / 497 (0.00%)	0 / 135 (0.00%)	2 / 135 (1.48%)
occurrences (all)	0	0	3
Rhinitis			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	2 / 135 (1.48%)
occurrences (all)	0	2	2
Upper respiratory tract infection			
subjects affected / exposed	10 / 497 (2.01%)	3 / 135 (2.22%)	5 / 135 (3.70%)
occurrences (all)	11	3	5
Urinary tract infection			
subjects affected / exposed	0 / 497 (0.00%)	2 / 135 (1.48%)	1 / 135 (0.74%)
occurrences (all)	0	2	1
Viral infection			

subjects affected / exposed occurrences (all)	2 / 497 (0.40%) 2	2 / 135 (1.48%) 2	1 / 135 (0.74%) 2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2020	The age of the study subject population was extended to 3 months of age and older. Clinical laboratory tests was updated to provide specific requirements for repeat laboratory assessments for alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and creatinine in the event of ≥30% increase from baseline value.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 March 2020	Study recruitment was paused for screening due to the COVID-19 pandemic.	01 June 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study recruitment was paused for screening due to COVID-19 starting 24 March 2020 and restarted on 01 June 2020. No additional disruptions occurred. As such, the impact to study conduct and study data were limited.

Notes: