



Clinical trial results:

A Phase 4, Multicenter, Open-Label Safety Study of Crisaborole Ointment 2% in Children Aged 3 Months to Less Than 24 Months With Mild to Moderate Atopic Dermatitis (AD)

Summary

EudraCT number	2019-002836-10
Trial protocol	Outside EU/EEA
Global end of trial date	12 April 2019

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	C3291002
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03356977
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 April 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the safety of crisaborole ointment 2% applied twice daily (BID) in children aged 3 months to less than 24 months 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 trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2018
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: 15
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	United States: 112
Worldwide total number of subjects	137
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)	137
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in the 3 countries from 16 January 2018 to 12 April 2019. A total of 137 subjects were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Crisaborole Topical Ointment, 2 Percent
-----------	---

Arm description:

Subjects with mild to moderate atopic dermatitis (AD) received crisaborole ointment, 2 percent on treatable AD lesions, twice daily from Day 1 to Day 29. Treatable AD lesions were identified at Baseline (Day 1) by investigator.

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

Dosage and administration details:

Crisaborole topical ointment, 2 percent to treatment targeted lesions, twice daily from Day 1 to Day 29.

Number of subjects in period 1	Crisaborole Topical Ointment, 2 Percent
Started	137
Completed	132
Not completed	5
WITHDRAWAL BY PARENT/GUARDIAN	2
Lost to follow-up	3

Baseline characteristics

Reporting groups

Reporting group title	Crisaborole Topical Ointment, 2 Percent
-----------------------	---

Reporting group description:

Subjects with mild to moderate atopic dermatitis (AD) received crisaborole ointment, 2 percent on treatable AD lesions, twice daily from Day 1 to Day 29. Treatable AD lesions were identified at Baseline (Day 1) by investigator.

Reporting group values	Crisaborole Topical Ointment, 2 Percent	Total	
Number of subjects	137	137	
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)	137	137	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: months			
arithmetic mean	13.6		
standard deviation	± 6.42	-	
Sex: Female, Male			
Units: Subjects			
Female	49	49	
Male	88	88	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	27	27	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	11	11	
White	84	84	
More than one race	13	13	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	16	16	
Not Hispanic or Latino	118	118	
Unknown or Not Reported	3	3	

End points

End points reporting groups

Reporting group title	Crisaborole Topical Ointment, 2 Percent
Reporting group description: Subjects with mild to moderate atopic dermatitis (AD) received crisaborole ointment, 2 percent on treatable AD lesions, twice daily from Day 1 to Day 29. Treatable AD lesions were identified at Baseline (Day 1) by investigator.	

Primary: Number of Subjects With Treatment Emergent Adverse Events (AEs), Serious Adverse Events (SAEs) and Site Reactions

End point title	Number of Subjects With Treatment Emergent Adverse Events (AEs), Serious Adverse Events (SAEs) and Site Reactions ^[1]
End point description: An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between first dose of investigational product and up to 28 days after the last dose of investigational product that were absent before treatment or that worsened relative to pretreatment state. AEs included both SAEs and non-SAEs. Site reactions are reactions which occurred in subjects at the site of application of investigational product. Safety analysis set included any subject who received at least 1 dose of investigational product.	
End point type	Primary

End point timeframe:

Baseline (Day 1) up to at least 28 days after last dose of investigational product (up to 60 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: subjects				
AEs	88			
SAEs	1			
Application site Reactions	15			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Height Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Height Values Meeting Pre-defined Criteria ^[2]
-----------------	--

End point description:

Height of subjects was measured in terms of centimeter (cm). The pre-defined criteria for measuring the height was less than (<) 55 cm and greater than (>) 92.5 cm. Safety analysis set included any subject who received at least 1 dose of investigational product. . Here, "Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	134			
Units: subjects				
< 55 cm	0			
> 92.5 cm	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Weight Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Weight Values Meeting Pre-defined Criteria ^[3]
-----------------	--

End point description:

Weight of subjects was measured in terms of kilogram (kg). The pre-defined criteria of measuring the weight of subjects was less than equal to (\leq) 4.5 kg and >15 kg. Safety analysis set included any subject who received at least 1 dose of investigational product. Here, "Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: subjects				
\leq 4.5 kg	0			
> 15 kg	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Blood Pressure Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Blood Pressure Values Meeting Pre-defined Criteria ^[4]
-----------------	--

End point description:

Diastolic Blood Pressure (DBP) and Systolic Blood Pressure (SBP) of subjects was measured in terms of millimeters of mercury (mmHg). The clinically significant pre-defined criteria were, SBP: change of greater than equal to (\geq) 30 mmHg increase from baseline (IFB) and SBP change of \geq 30 mmHg decrease from baseline (DFB); DBP: change of \geq 20 mmHg IFB and DBP change of \geq 20 mmHg DFB. Safety analysis set included any subject who received at least 1 dose of investigational product. Here, "Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint and "n" signifies subjects evaluable for specific rows.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	136			
Units: subjects				
SBP: change of \geq 30 mmHg IFB (n=136)	3			
SBP: change of \geq 30 mmHg DFB (n=136)	4			
DSBP: change of \geq 20 mmHg IFB (n=135)	8			
DSBP: change of \geq 20 mmHg DFB (n=135)	18			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Pulse Rate Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Pulse Rate Values Meeting Pre-defined Criteria ^[5]
-----------------	--

End point description:

Pulse rate of subjects was measured in terms of beats per minute (bpm). The pre-defined criteria of measuring the pulse rate of subjects was <90 bpm and >180 bpm. Safety analysis set included any subject who received at least 1 dose of investigational product.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: subjects				
<90 bpm	12			
>180 bpm	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Respiratory Rate Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Respiratory Rate Values Meeting Pre-defined Criteria ^[6]
-----------------	--

End point description:

Respiratory rate was measured in terms of number of breaths per minute. The pre-defined criteria of measuring the respiratory rate of subjects was < 22 breaths per min and > 53 breaths per min. Safety analysis set included any subject who received at least 1 dose of investigational product.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1), Day 8, Day 15, Day 29 (end of treatment)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: subjects				
< 22 breaths per minute	17			
> 53 breaths per minute	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Body Temperature Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Body Temperature Values Meeting Pre-defined Criteria ^[7]
-----------------	--

End point description:

Body temperature of subjects was measured in degree Celsius. The normal body temperature value was ≥ 39 degree Celsius. Safety analysis set included any subject received at least 1 dose of investigational product.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Change From Baseline in Electrocardiogram (ECG) Values Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Change From Baseline in Electrocardiogram (ECG) Values Meeting Pre-defined Criteria ^[8]
-----------------	---

End point description:

ECG of subjects was measured in terms of millisecond (msec). ECG parameters included pulse rate (PR) interval, QRS interval, corrected QT interval using Fridericia's formula (QTcF). ECG values meeting pre-defined criteria were 1) PR interval: greater than equal to (\geq) 25 percent (%) increase when baseline greater than ($>$) 200 milliseconds (msec); or increase $\geq 50\%$ when baseline less than or equal to (≤ 200) msec; 2) QRS interval: $\geq 25\%$ increase when baseline > 100 msec; $\geq 50\%$ increase when baseline ≤ 100 msec; 3) QTcF interval: QTc interval using Fridericia's formula (QTcF interval) > 30 msec. IFB stands for increase from baseline. Safety analysis set included any subject who received at least 1 dose of investigational product. Here, "Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	135			
Units: subjects				
PR Interval: > 200 msec and >=25% IFB	0			
PR Interval: <= 200 msec and >=50% IFB	1			
QRS Duration: < 100 msec and >= 50% IFB	0			
QRS Duration: >= 100 msec and >= 25% IFB	0			
QTcF Interval: >30 msec	10			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Laboratory Parameters Meeting Pre-defined Criteria

End point title	Number of Subjects With Clinically Significant Laboratory Parameters Meeting Pre-defined Criteria ^[9]
-----------------	--

End point description:

Criteria: hematology: hemoglobin, hematocrit, erythrocytes < 0.8*lower limit of normal (LLN), platelets <0.5*LLN >1.75*upper limit of normal (ULN), leukocytes <0.6* LLN >1.5* ULN, lymphocytes, lymphocytes/leukocytes, neutrophils, neutrophils/leukocytes <0.8* LLN >1.2* ULN, basophils, basophils/leukocytes, eosinophils, eosinophils/leukocytes monocytes monocytes/leukocytes >1.2*ULN. Clinical chemistry: bilirubin >1.5*ULN, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase >3.0*ULN, protein, albumin <0.8* LLN >1.2* ULN, blood urea nitrogen, creatinine >1.3* ULN, sodium <0.95*LLN >1.05*ULN, potassium, chloride, bicarbonate <0.9* LLN >1.1* ULN, glucose <0.6*LLN >1.5*ULN. Safety analysis set included any subject who received >=1 dose of investigational product. Here, "Number of Subjects Analysed" signifies subjects who were evaluable for this endpoint.

End point type	Primary
----------------	---------

End point timeframe:

Baseline (Day 1) up to Day 29 (end of treatment)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Crisaborole Topical Ointment, 2 Percent			
Subject group type	Reporting group			
Number of subjects analysed	122			
Units: subjects	105			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day 1) up to at least 28 days after last dose of investigational product (up to 60 days)

Adverse event reporting additional description:

Same event may appear as both an adverse event (AE) and serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	21.1
--------------------	------

Reporting groups

Reporting group title	Crisaborole Topical Ointment, 2 Percent
-----------------------	---

Reporting group description:

Subjects with mild to moderate AD received crisaborole ointment, 2 percent on treatable AD lesions, twice daily from Day 1 to Day 29. Treatable AD lesions were identified at Baseline (Day 1) by investigator.

Serious adverse events	Crisaborole Topical Ointment, 2 Percent		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 137 (0.73%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Crisaborole Topical Ointment, 2 Percent		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 137 (29.93%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	13 / 137 (9.49%)		
occurrences (all)	13		

Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	10 / 137 (7.30%) 10		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 137 (5.11%) 7		
Skin and subcutaneous tissue disorders Dermatitis atopic subjects affected / exposed occurrences (all) Dermatitis diaper subjects affected / exposed occurrences (all)	9 / 137 (6.57%) 9 9 / 137 (6.57%) 9		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	10 / 137 (7.30%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2018	Added that any subject with a new or ongoing adverse event at the time of the Day 57 (end of study) follow-up contact, should be seen in the clinic for evaluation of that adverse event.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported