Clinical trial results:
An Open-Label, Long-Term Extension Study to Evaluate the Safety of Cortexolone 17-Propionate (CB-03-01) Cream, 1% Applied Twice-Daily in Subjects with Acne Vulgaris

Summary

EudraCT number	2015-002637-21
Trial protocol	RO BG PL
Global end of trial date	31 August 2018

Results information

Result version number	v1 (current)
This version publication date	27 November 2020
First version publication date	27 November 2020

Trial information

Trial identification

Sponsor protocol code	CB-03-01/27

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02682264
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cassiopea SpA
Sponsor organisation address	Via C. Colombo 1 , Lainate (MI), Italy, 20045
Public contact	Cassiopea Research & Development, CASSIOPEA SpA, +39 02868 91 124, R&D@cassiopea.com
Scientific contact	Cassiopea Research & Development, CASSIOPEA SpA, +39 02868 91 124, R&D@cassiopea.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	28 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2018
Global end of trial reached?	Yes
Global end of trial date	31 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the long-term safety of CB-03-01 cream, 1% applied twice daily for an additional nine months in subjects with acne vulgaris that participated in the Phase 3 pivotal studies for a total treatment of up to 12 months.
This was a multicenter, open label, long-term extension study for CB-03-01 cream, 1% focused on safety in male and female participants, 9 years or older who completed one of the Phase 3 pivotal studies [CB-03-01/25 and CB-03-01/26]. Participants applied the active medication (CB-03-01 cream, 1%) twice daily to the entire face and, if designated by investigator AND desired by the participant, truncal acne for nine additional months of treatment. Thus, overall participants were exposed to CB-03-01 cream, 1% for a total treatment of up to 12 months (0 or 3 months in the Phase 3 pivotal study and an additional nine months in this long-term safety study).

Protection of trial subjects:

Male and female subjects 9 years of age or older who were enrolled and completed participation in one of the Phase 3 pivotal studies (CB-03-01/25 and CB-03-01/26) were enrolled in this study from study centers in the US, Poland, Bulgaria, Ukraine, Romania, Serbia, and Republic of Georgia. Interested individuals were given an opportunity to discuss the procedures involved in study participation with the site staff and the principal investigator. An IRB/IEC/LEC-approved informed consent/assent form and subject instruction sheet was given to the potential subject and an opportunity afforded to read , discuss and understand the consent/assent form and ask questions.
This study was conducted in accordance with principles of the Declaration of Helsinki (7th revision), with the current Good Clinical Practice guidelines (ICH E6, Revision 2) and with other applicable regulations.
The investigators and all study staff conducted the study in compliance with the study protocol.
The rights, safety, and well-being of the study subjects were the most important considerations and prevailed over the interests of science and society.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 134
Country: Number of subjects enrolled	Romania: 73
Country: Number of subjects enrolled	Bulgaria: 48
Country: Number of subjects enrolled	United States: 242
Country: Number of subjects enrolled	Ukraine: 56
Country: Number of subjects enrolled	Georgia: 30

Country: Number of subjects enrolled	Serbia: 26
Worldwide total number of subjects	609
EEA total number of subjects	255

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	9
Adolescents (12-17 years)	304
Adults (18-64 years)	296
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 609 subjects who were rolled over (i.e., enrolled) from the two Phase 3 pivotal studies (CB-03-01/25 and CB-03-01/26) into this long-term, safety study. However, two (2) subjects in the original vehicle cream were not treated with test article and thus were excluded from the study population (Safety set).

Pre-assignment

Screening details:

not applicable

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CB-03-01 1% cream

Arm description:

Subjects in this arm received CB-03-01 (cortexolone 17α-propionate) Cream, 1% in the pivotal study and continued their CB-03-01 cream treatment in this open-label safety extension study. Subjects were instructed to apply CB-03-01 Cream, 1%, twice daily to whole face (about 1 gram) and affected areas of trunk (if applicable) for up to an additional 9 months. Over the course of the study, treatment on the face and/or trunk may be discontinued if/when acne clears and re-started if/when acne worsens, according to the assessment of the investigator for each respective treatment area.

Cortexolone 17α-propionate (USAN/INN: clascoterone) is an androgen receptor inhibitor that is being developed as a 1% cream for the topical treatment of acne vulgaris.

Arm type	CB-03-01
Investigational medicinal product name	Clascoterone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Participants applies the active medication (CB-03-01 cream, 1%) twice daily to the entire face and, if designated by investigator AND desired by the participant, truncal acne for nine additional months of treatment. Thus, overall participants were exposed to CB-03-01 cream, 1% for a total treatment of up to 12 months (0 or 3 months in the Phase 3 pivotal study and an additional nine months in this long-term safety study).
Participants treated facial acne per protocol for nine months. Treatment of truncal acne was discussed by the investigator and participant. Treatment on the face and/or trunk was discontinued if/when acne clears and re-started if/when acne worsens, according to the assessment of the investigator for each respective treatment area.

Arm title	CB-03-01 Cream, 1% (Vehicle Arm)

Arm description:

Subjects in this arm received vehicle cream in the pivotal study and CB-03-01 cream in this open-label safety extension study.

Arm type	CB-03-01 (vehicle)

No investigational medicinal product assigned in this arm

Number of subjects in period 1[1]	CB-03-01 1% cream	CB-03-01 Cream, 1% (Vehicle Arm)
Started	317	290
Completed	179	168
Not completed	138	122
Withdrawal by Parents	6	7
Consent withdrawn by subject	56	45
Recovery	1	2
Adverse event, non-fatal	9	-
Technical problems	-	1
Pregnancy	1	2
Stopped Test Article application	-	1
Moved abroad and unable to continue	-	3
Non compliance with study Drug	1	4
Lost to follow-up	49	41
Progressive disease	1	-
Lack of efficacy	14	16

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: there were 609 subjects who were rolled over (i.e., enrolled) from the two Phase 3 pivotal studies (CB-03-01/25 and CB-03-01/26) into this long-term, safety study. However, two (2) subjects in the original vehicle cream were not treated with test article and thus were excluded from the study population (Safety set).

Baseline characteristics

Reporting groups

Reporting group title	CB-03-01 1% cream

Reporting group description:

Subjects in this arm received CB-03-01 (cortexolone 17α-propionate) Cream, 1% in the pivotal study and continued their CB-03-01 cream treatment in this open-label safety extension study. Subjects were instructed to apply CB-03-01 Cream, 1%, twice daily to whole face (about 1 gram) and affected areas of trunk (if applicable) for up to an additional 9 months. Over the course of the study, treatment on the face and/or trunk may be discontinued if/when acne clears and re-started if/when acne worsens, according to the assessment of the investigator for each respective treatment area.

Cortexolone 17α-propionate (USAN/INN: clascoterone) is an androgen receptor inhibitor that is being developed as a 1% cream for the topical treatment of acne vulgaris.

Reporting group title	CB-03-01 Cream, 1% (Vehicle Arm)

Reporting group description:

Subjects in this arm received vehicle cream in the pivotal study and CB-03-01 cream in this open-label safety extension study.

Reporting group values	CB-03-01 1% cream	CB-03-01 Cream, 1% (Vehicle Arm)	Total
Number of subjects	317	290	607
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	19.2	19.3	
standard deviation	± 5.8	± 6.7	-
Gender categorical Units: Subjects			
Female	198	183	381
Male	119	107	226
Ethnicity Units: Subjects			
Hispanic or Latino	27	15	42
Not Hispanic or Latino	290	275	565
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	6	8	14
Native Hawaiian or Other Pacific Islander	2	1	3
Black or African American	17	18	35
White	283	256	539
More than one race	4	6	10
Unknown or Not Reported	4	1	5

Subject analysis sets

Subject analysis set title	Safety Analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population defined as all subjects who applied at least one dose of test article.
There were 609 subjects who were rolled over (i.e., enrolled) from the two Phase 3 pivotal studies (CB-03-01/25 and CB-03-01/26) into this long-term, safety study. However, two (2) subjects in the original vehicle cream were not treated with test article and thus were excluded from the study population (Safety set).

Reporting group values	Safety Analysis		
Number of subjects	607		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	19.2		
standard deviation	± 6.3		
Gender categorical Units: Subjects			
Female	381		
Male	226		
Ethnicity Units: Subjects			
Hispanic or Latino	42		
Not Hispanic or Latino	565		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	14		
Native Hawaiian or Other Pacific Islander	3		
Black or African American	35		
White	539		
More than one race	10		
Unknown or Not Reported	5		

End points

End points reporting groups

Reporting group title	CB-03-01 1% cream

Reporting group description:

Subjects in this arm received CB-03-01 (cortexolone 17α-propionate) Cream, 1% in the pivotal study and continued their CB-03-01 cream treatment in this open-label safety extension study. Subjects were instructed to apply CB-03-01 Cream, 1%, twice daily to whole face (about 1 gram) and affected areas of trunk (if applicable) for up to an additional 9 months. Over the course of the study, treatment on the face and/or trunk may be discontinued if/when acne clears and re-started if/when acne worsens, according to the assessment of the investigator for each respective treatment area.

Cortexolone 17α-propionate (USAN/INN: clascoterone) is an androgen receptor inhibitor that is being developed as a 1% cream for the topical treatment of acne vulgaris.

Reporting group title	CB-03-01 Cream, 1% (Vehicle Arm)

Reporting group description:

Subjects in this arm received vehicle cream in the pivotal study and CB-03-01 cream in this open-label safety extension study.

Subject analysis set title	Safety Analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population defined as all subjects who applied at least one dose of test article.
There were 609 subjects who were rolled over (i.e., enrolled) from the two Phase 3 pivotal studies (CB-03-01/25 and CB-03-01/26) into this long-term, safety study. However, two (2) subjects in the original vehicle cream were not treated with test article and thus were excluded from the study population (Safety set).

Primary: Incidence of Any Local and Systemic Treatment Emergent AEs (TEAEs)

End point title	Incidence of Any Local and Systemic Treatment Emergent AEs (TEAEs)[1]

End point description:

Number of subjects with any local and systemic treatment emergent AEs (TEAEs)

End point type	Primary

End point timeframe:

up to 52 weeks

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: Descriptive statistics . All AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 18.1 and listed. Individual TEAEs (i.e., all the AEs occurring or worsening after the first dose of the test article) were listed, documenting course, severity, relationship to test article, and outcome. The number and percentage of subjects with any TEAE and the number of TEAEs were presented overall and were tabulated by MedDRA system organ class (SOC) and by preferred term (PT).

End point values	CB-03-01 1% cream	CB-03-01 Cream, 1% (Vehicle Arm)	Safety Analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	317	290	607	
Units: Number of subjects with TEAE(s)	58	52	110	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events (TEAEs) and serious adverse events (SAEs) were collected from Baseline (Long-term study Day 1) and up to Long-term study month 9/early termination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	CB-03-01 Cream, 1%

Reporting group description:

Subjects in this arm received CB-03-01 (cortexolone 17α-propionate) Cream, 1% in the pivotal study and continued their CB-03-01 cream treatment in this open-label safety extension study. Subjects were instructed to apply CB-03-01 Cream, 1%, twice daily to whole face (about 1 gram) and affected areas of trunk (if applicable) for up to an additional 9 months. Over the course of the study, treatment on the face and/or trunk may be discontinued if/when acne clears and re-started if/when acne worsens, according to the assessment of the investigator for each respective treatment area.

Cortexolone 17α-propionate (USAN/INN: clascoterone) is an androgen receptor inhibitor that is being developed as a 1% cream for the topical treatment of acne vulgaris.

Reporting group title	CB-03-01 Cream, 1% (Vehicle Arm)

Reporting group description:

Subjects in this arm received vehicle cream in the pivotal study and CB-03-01 cream in this open-label safety extension study.

Serious adverse events	CB-03-01 Cream, 1%	CB-03-01 Cream, 1% (Vehicle Arm)	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 317 (1.26%)	3 / 290 (1.03%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Coronary artery dissection			
subjects affected / exposed	0 / 317 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 317 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 317 (0.32%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 317 (0.00%)	1 / 290 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastroenteritis eosinophilic			
subjects affected / exposed	1 / 317 (0.32%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 317 (0.32%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 317 (0.32%)	0 / 290 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.7 %

Non-serious adverse events	CB-03-01 Cream, 1%	CB-03-01 Cream, 1% (Vehicle Arm)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 317 (6.62%)	17 / 290 (5.86%)	
General disorders and administration site conditions			
Application site acne			
subjects affected / exposed	4 / 317 (1.26%)	0 / 290 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	6 / 317 (1.89%)	10 / 290 (3.45%)	
occurrences (all)	7	13	
Respiratory tract infection viral			
subjects affected / exposed	1 / 317 (0.32%)	4 / 290 (1.38%)	
occurrences (all)	1	4	
Sinusitis			
subjects affected / exposed	3 / 317 (0.95%)	2 / 290 (0.69%)	
occurrences (all)	3	2	
Upper respiratory tract infection			
subjects affected / exposed	7 / 317 (2.21%)	1 / 290 (0.34%)	
occurrences (all)	8	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported