Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Vehicle-Controlled Study to Evaluate the Safety and Efficacy of Cortexolone 17-Propionate (CB-03-01) 1% Cream Applied Twice-Daily for 12 Weeks in Subjects with Facial Acne Vulgaris

Summary

EudraCT number	2015-002623-26
Trial protocol	BG RO
Global end of trial date	21 February 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-03-01/26

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02608476
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cassiopea SpA
Sponsor organisation address	Via C. Colombo 1 , Linate , Italy,
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	03 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2018
Global end of trial reached?	Yes
Global end of trial date	21 February 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 safety and efficacy of CB-03-01 cream, 1%, versus the vehicle cream applied twice daily for 12 weeks in subjects with facial acne vulgaris.

Protection of trial subjects:

Approval on the conduct of the trial was obtained by the national Ethic Committee, by the central IRB or by the IEC of each participating center and by the relevant Competent Authorities (CAs).
Subject selection or any other study-related procedures did not commence until approval from both involved CAs and IECs according to the local regulations of the involved countries had been obtained.
The study protocol, the subject information leaflet and the informed consent/assent document were submitted to the national Independent Ethics Committee (IEC) of Bulgaria, Romania and Poland and to the IEC of each center participating in the study in Serbia and Republic of Georgia.
For all US sites, the study protocol, consent/assent form, participant recruitment materials/process, and other relevant documents were submitted to a central IRB and approval obtained in compliance with the requirements set forth in Title 21 of the Code of Federal Regulations (CFR), Parts 56.107 to 56.115
The study was conducted under the provisions of the Declaration of Helsinki, (64th WMA General Assembly, Fortaleza, Brazil, October 2013 for EU and 7th revision for US), and in accordance with the International Conference on Harmonization (ICH) Consolidated Guideline on Good Clinical Practice (GCP) (EMA/CHMP/ICH/135/1995 E6(R1) of July 2002 and E6(R2) of December 2016) and with other applicable regulations
Male and female subjects 9 years of age or older with moderate to severe facial acne vulgaris (Grade 3 or 4 on Investigator’s Global Assessment [IGA]) were recruited as subjects from study centers in Bulgaria, Republic of Georgia, Poland, Romania, Serbia and US. Interested individuals were given an opportunity to discuss the activities involved in study participation with the site staff and the principal investigator. An IRB- or IEC-approved informed consent/assent form and subject instruction sheet were given to the potential subject and an opportunity afforded to read the consent/assent fo

Background therapy:

no background therapy was planned

Evidence for comparator:

no comparator were used in the study

Actual start date of recruitment	16 November 2015
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: 222
Country: Number of subjects enrolled	Romania: 186
Country: Number of subjects enrolled	Bulgaria: 90
Country: Number of subjects enrolled	Georgia: 102

Country: Number of subjects enrolled	United States: 93
Country: Number of subjects enrolled	Serbia: 39
Worldwide total number of subjects	732
EEA total number of subjects	498

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)	3
Adolescents (12-17 years)	341
Adults (18-64 years)	388
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients recruited by investigators in their research sites from the database or by means of website advertisement or reference from other doctors. Patients underwent screening procedures and were required to meet all the inclusion criteria and none of the exclusion criteria.

Pre-assignment

Screening details:

A total of 756 subjects were screened and 732 of them were randomized to the assigned treatment, whereas 24 subjects were screening failures: 369 subjects were randomised to receive CB-03-01 and 363 were randomised to receive vehicle

Period 1

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

Blinding implementation details:

Subjects who were eligible for enrollment into the study were randomized to receive CB-03-01 cream or vehicle cream in a 1:1 ratio
The randomization scheme was blocked by investigational site. At each site, subject kits were dispensed according to the kit number assigned by an Interactive Voice Response System/Interactive Web Response System (IVRS/IWRS) as subjects were enrolled

Arms

Are arms mutually exclusive?	Yes
Arm title	clascoterone cream 1%

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clascoterone cream 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

The twice daily application of clascoterone Cream 1% (1gr each application) for 12 weeks
Cream was applied in the morning and in the evening 30 minutes before to go to bed .

Arm title	Vehicle

Arm description: -

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

Dosage and administration details:

About 1 gram of the cream was applied to the face twice daily (in the morning and in the evening).

Number of subjects in period 1	clascoterone cream 1%	Vehicle
Started	369	363
Completed	302	282
Not completed	67	81
Consent withdrawn by subject	30	37
Physician decision	1	-
Adverse event, non-fatal	2	8
Consent withdrawn by parents/guardians	5	4
Pregnancy	-	1
had progressive disease	1	-
poor compliance	1	5
Lost to follow-up	24	24
Lack of efficacy	3	1
other reason	-	1

Baseline characteristics

Reporting groups	
Reporting group title	clascoterone cream 1%
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	

Reporting group values	clascoterone cream 1%	Vehicle	Total
Number of subjects	369	363	732
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	19.3	19.0	
standard deviation	± 5.6	± 5.4	-
Gender categorical Units: Subjects			
Female	243	221	464
Male	126	142	268
ethnicity Units: Subjects			
Hispanic or Latino	20	9	29
Not Hispanic or Latino	349	354	703
Race Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	0	4	4
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	7	6	13
White	357	348	705
More than one race	0	1	1
Unknown or Not Reported	4	2	6
Baseline IGA Units: Subjects			
0-Clear	0	0	0
1-Almost clear	0	0	0
2-Mild	0	0	0
3-Moderate	305	313	618
4-Severe	64	50	114
Baseline Acne Lesion Count			
Not InFlammatory Lesion			
Units: Lesion			
arithmetic mean	62.8	63.3	
standard deviation	± 21.4	± 20.5	-
Baseline Acne Lesion Count			

Inflammatory Lesion			
Units: Lesion			
arithmetic mean	42.9	41.3	
standard deviation	± 12.2	± 11.0	-
Baseline Acne Lesion Count			
Total Lesion			
Units: Lesion			
arithmetic mean	105.7	104.6	
standard deviation	± 25.8	± 24.2	-

End points

End points reporting groups

Reporting group title	clascoterone cream 1%
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	
Subject analysis set title	Efficacy Analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention-to -treat (ITT) set includes all randomized subjects	

Primary: Investigator's Global Assessment (IGA) "Success" at week 12

End point title	Investigator's Global Assessment (IGA) "Success" at week 12
End point description:	
Proportion of subjects in each treatment group who achieved "success" at week 12, with "success" defined as an IGA score of "clear (score=0)" or "almost clear (score=1)" AND at least a two-point reduction in IGA compared to baseline.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: % IGA success				
number (not applicable)	20.3	6.5		

Statistical analyses

Statistical analysis title	IGA "Success" at week 12
Statistical analysis description:	
A logistic regression model with treatment and analysis center as fixed effects was used to compare the proportion of subjects in each treatment group with at least a two-point reduction in IGA AND an IGA score of 0 (clear) or 1 (almost clear) at week 12. The adjusted odds ratio of the comparison between groups and its 95% confidence interval (CI) were derived from the regression model	
Comparison groups	Vehicle v clascoterone cream 1%
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Regression, Logistic

Primary: Absolute change from baseline in Non Inflammatory Lesion Count (NILC) at week 12

End point title	Absolute change from baseline in Non Inflammatory Lesion Count (NILC) at week 12

End point description:

Absolute change from baseline in NILC in each treatment group at week 12.

End point type	Primary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: change from baseline				
arithmetic mean (confidence interval 95%)	-19.4 (-22.1 to -16.7)	-10.8 (-13.6 to -8.0)		

Statistical analyses

Statistical analysis title	Absolute change from baseline in NILC at week 12

Statistical analysis description:

An analysis of covariance (ANCOVA) model was used to compare the absolute change from baseline in non-inflammatory lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline non-inflammatory lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model.

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Primary: Absolute change from baseline in Inflammatory Lesion Count (ILC) at week 12

End point title	Absolute change from baseline in Inflammatory Lesion Count (ILC) at week 12

End point description:

Absolute change from baseline in ILC in each treatment group at week 12.

End point type	Primary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: change from baseline				
arithmetic mean (confidence interval 95%)	-20.0 (-21.7 to -18.3)	-12.6 (-14.3 to -10.8)		

Statistical analyses

Statistical analysis title	Absolute change from baseline in ILC at week 12

Statistical analysis description:

An ANCOVA model was used to compare the absolute change from baseline in inflammatory lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline inflammatory lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Absolute change from baseline in Total Lesion Count (TLC) at week 12.

End point title	Absolute change from baseline in Total Lesion Count (TLC) at week 12.

End point description:

Absolute change from baseline in TLC in each treatment group at week 12.

End point type	Secondary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: change from baseline				
arithmetic mean (confidence interval 95%)	-40.0 (-43.8 to -36.2)	-23.6 (-27.8 to -19.5)		

Statistical analyses

Statistical analysis title	Absolute change from baseline in TLC at week 12

Statistical analysis description:

An ANCOVA model was used to compare the absolute change from baseline in total lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline total lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Percent change from baseline in Total Lesion Count (TLC) at week 12.

End point title	Percent change from baseline in Total Lesion Count (TLC) at week 12.

End point description:

Percent change from baseline in TLC in each treatment group at week 12.

End point type	Secondary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: % change from baseline				
arithmetic mean (confidence interval 95%)	-37.3 (-41.1 to -33.6)	-22.1 (-26.1 to -18.1)		

Statistical analyses

Statistical analysis title	Percent change in TLC at week12

Statistical analysis description:

An ANCOVA model was used to compare the percent change from baseline in total lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline total lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Percent change from baseline in Non Inflammatory Lesion Count (NILC) at week 12.

End point title	Percent change from baseline in Non Inflammatory Lesion Count (NILC) at week 12.

End point description:

Percent change from baseline in NILC in each treatment group at week 12.

End point type	Secondary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: % of Change from Baseline				
arithmetic mean (confidence interval 95%)	-29.3 (-33.7 to -24.9)	-15.6 (-20.3 to -10.9)		

Statistical analyses

Statistical analysis title	Percent change from baseline in NILC at week12

Statistical analysis description:

An ANCOVA model was used to compare the percentage change from baseline in noninflammatory lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline non-inflammatory lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Secondary: Percent change from baseline in Inflammatory Lesion Count (ILC) at week 12.

End point title	Percent change from baseline in Inflammatory Lesion Count (ILC) at week 12.

End point description:

Percent change from baseline in ILC in each treatment group at week 12.

End point type	Secondary

End point timeframe:

12 weeks

End point values	clascoterone cream 1%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	363		
Units: % of Change from Baseline				
arithmetic mean (confidence interval 95%)	-46.9 (-50.9 to -42.8)	-29.6 (-33.9 to -25.3)		

Statistical analyses

Statistical analysis title	Percent change from baseline in ILC at week 12

Statistical analysis description:

An ANCOVA model was used to compare the percentage change from baseline in inflammatory lesion counts in each treatment group at week 12, with treatment and analysis center as fixed effects and the baseline inflammatory lesion counts as covariate. The adjusted means difference of the comparison between groups and its 95% CI were derived from the regression model.

Comparison groups	clascoterone cream 1% v Vehicle
Number of subjects included in analysis	732
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and serious adverse events (SAEs) were collected from screening visit, Baseline (Day 1)
and up to Week 12/early termination

Adverse event reporting additional description:

Treatment-emergent AEs (TEAEs) are AEs collected from the date of the first dose of IMP until the date of the final study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	clascoterone 1% cream

Reporting group description: -

Reporting group title	vehicle

Reporting group description: -

Serious adverse events	clascoterone 1% cream	vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 369 (0.00%)	1 / 363 (0.28%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
severe hematoma of the right thigh			
subjects affected / exposed	0 / 369 (0.00%)	1 / 363 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.8 %

Non-serious adverse events	clascoterone 1% cream	vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 369 (5.69%)	34 / 363 (9.37%)	
Nervous system disorders			
headache			
subjects affected / exposed	4 / 369 (1.08%)	3 / 363 (0.83%)	
occurrences (all)	4	3	

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 369 (0.00%)	3 / 363 (0.83%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 369 (0.54%)	3 / 363 (0.83%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 369 (0.00%)	3 / 363 (0.83%)	
occurrences (all)	0	3	
Oropharingeal pain			
subjects affected / exposed	4 / 369 (1.08%)	4 / 363 (1.10%)	
occurrences (all)	4	6	
Rhinorrhoea			
subjects affected / exposed	3 / 369 (0.81%)	5 / 363 (1.38%)	
occurrences (all)	3	5	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 369 (0.27%)	3 / 363 (0.83%)	
occurrences (all)	1	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 369 (0.81%)	0 / 363 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	3 / 369 (0.81%)	7 / 363 (1.93%)	
occurrences (all)	3	10	
Upper respiratory tract infection			
subjects affected / exposed	1 / 369 (0.27%)	4 / 363 (1.10%)	
occurrences (all)	1	4	

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