



## 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) Cream, 1% Applied Twice Daily for 12 Weeks in Subjects with Facial Acne Vulgaris

#### Summary

EudraCT number	2023-000463-32
Trial protocol	Outside EU/EEA
Global end of trial date	11 April 2018

#### Results information

Result version number	v1 (current)
This version publication date	27 May 2023
First version publication date	27 May 2023

#### Trial information

##### Trial identification

Sponsor protocol code	CB-03-01/25
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02608450
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Cassiopea SpA
Sponsor organisation address	Via C. Colombo 1, Linate, Italy, 20045
Public contact	Cassiopea SpA, Cosmo SpA, +39 02868 91124, dermatology@cosmopharma.com
Scientific contact	Cassiopea SpA, Cosmo SpA, +39 02868 91124, dermatology@cosmopharma.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-003330-PIP01-22
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	17 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 April 2018
Global end of trial reached?	Yes
Global end of trial date	11 April 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:

The study protocol, consent/assent form, participant recruitment materials/process, and other relevant documents were submitted for review and approval prior to study initiation to a central or local Institutional Review Board (IRB) for all US sites, and to an Independent Ethics Committee (IEC) for Republic of Georgia sites and to a Local Ethics Committee (LEC) for Ukraine sites. The IRB approval complied with the requirements set forth in Title 21 of the Code of Federal Regulations (CFR), Parts 56.107 to 56.115. The approval of the consent/assent in Republic of Georgia and Ukraine complied with local legislation and international standards.

The study was conducted in accordance with principles of the Declaration of Helsinki, with the current Good Clinical Practice (GCP) Guideline and with other applicable regulations.

Background therapy:

No background therapy was planned

Evidence for comparator:

No comparators were used in the study

Actual start date of recruitment	21 January 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	United States: 502
Country: Number of subjects enrolled	Georgia: 74
Country: Number of subjects enrolled	Ukraine: 132
Worldwide total number of subjects	708
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	16
Adolescents (12-17 years)	300
Adults (18-64 years)	392
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

There were 825 subjects screened for this study; 708 subjects were enrolled, and 117 subjects were screen failures. Of the 708 enrolled subjects, 353 subjects were randomized to treatment with CB-03-01 and 355 subjects were randomized to treatment with Vehicle.

### Period 1

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

Blinding implementation details:

Subjects who are eligible for enrollment into the study will be randomized to receive CB-03-01 cream or vehicle cream in a 1:1 ratio. The system automatically assigned the lowest available study drug kit number available at the site containing the treatment to which the subject was randomized. Treatment group designation remained blinded until the final database was locked.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	CB-03-01 Cream

Arm description:

CB-03-01 cream, 1% applied twice daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	CB-03-01 Cream, 1%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Twice daily application of CB-03-01 Cream, 1% (about 1 gram) for 12 weeks.

<b>Arm title</b>	Vehicle Cream
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Arm description:

Vehicle cream applied twice daily for 12 weeks

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:

Twice daily application of Vehicle Cream (about 1 gram) for 12 weeks

<b>Number of subjects in period 1</b>	CB-03-01 Cream	Vehicle Cream
Started	353	355
Completed	287	290
Not completed	66	65
Withdrawal by parent	2	3
Consent withdrawn by subject	21	15
Physician decision	-	1
Adverse event, non-fatal	3	6
Pregnancy	-	1
Noncompliance with study drug	-	2
Lost to follow-up	39	32
Progressive disease	1	-
Multiple reasons	-	2
Lack of efficacy	-	3

## Baseline characteristics

### Reporting groups

Reporting group title	CB-03-01 Cream
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Reporting group description:

CB-03-01 cream, 1% applied twice daily for 12 weeks

Reporting group title	Vehicle Cream
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Reporting group description:

Vehicle cream applied twice daily for 12 weeks

Reporting group values	CB-03-01 Cream	Vehicle Cream	Total
Number of subjects	353	355	708
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	20.0	19.9	
standard deviation	± 6.7	± 6.8	-
Gender categorical			
Units: Subjects			
Female	221	215	436
Male	132	140	272
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	94	80	174
Not Hispanic or Latino	259	275	534
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	9	10	19
Native Hawaiian or Other Pacific Islander	2	0	2
Black or African American	31	38	69
White	298	297	595
More than one race	9	7	16
Not recorded	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	292	291	583
4 - Severe	61	64	125
Baseline Acne Lesions Counts			
Non-inflammatory Lesions			
Units: Lesions			
arithmetic mean	59.1	60.7	
standard deviation	± 22.2	± 22.1	-

Baseline Acne Lesion Counts			
Inflammatory Lesions			
Units: Lesions			
arithmetic mean	42.4	42.9	
standard deviation	± 11.8	± 12.3	-
Baseline Acne Lesion Counts			
Total Lesions			
Units: Lesions			
arithmetic mean	101.5	103.6	
standard deviation	± 25.1	± 26.1	-

## End points

### End points reporting groups

Reporting group title	CB-03-01 Cream
Reporting group description: CB-03-01 cream, 1% applied twice daily for 12 weeks	
Reporting group title	Vehicle Cream
Reporting group description: Vehicle cream applied twice daily for 12 weeks	
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: Percentage of subjects in each treatment group achieving "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	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: % of participants				
number (not applicable)	18.4	9.0		

### 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 achieving success in each treatment group at Week 12, where "success" was defined as an IGA score of "clear (score=0)" or "almost clear (score=1)" AND at least a two-point improvement in IGA compared to Baseline.	
Comparison groups	CB-03-01 Cream v Vehicle Cream



Number of subjects included in analysis	708
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)

End point title	Absolute Change From Baseline in Non-inflammatory Lesion Count (NILC)
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	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: Change from Baseline				
arithmetic mean (confidence interval 95%)	-19.4 (-22.6 to -16.7)	-13.0 (-15.7 to -10.3)		

### 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.
Comparison groups	Vehicle Cream v CB-03-01 Cream
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

### Primary: Absolute Change From Baseline in Inflammatory Lesion Count (ILC)

End point title	Absolute Change From Baseline in Inflammatory Lesion Count (ILC)
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	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: Change from Baseline				
arithmetic mean (confidence interval 95%)	-19.3 (-21.1 to -17.5)	-15.5 (-17.3 to -13.6)		

## Statistical analyses

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

An ANCOVA 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.

Comparison groups	CB-03-01 Cream v Vehicle Cream
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

## Secondary: Absolute Change From Baseline in Total Lesion Count (TLC)

End point title	Absolute Change From Baseline in Total Lesion Count (TLC)
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End point description:

Absolute change from Baseline in TLC in each treatment group at Week 12.

End point type	Secondary
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End point timeframe:

12 weeks

End point values	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: Total Lesions				
arithmetic mean (confidence interval 95%)	-39.1 (-43.0 to -35.1)	-28.8 (-32.6 to -24.9)		

## Statistical analyses

<b>Statistical analysis title</b>	Absolute Change from Baseline in TLC at week 12
Statistical analysis description: An ANCOVA 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.	
Comparison groups	CB-03-01 Cream v Vehicle Cream
Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

## Secondary: Percent Change From Baseline in Total Lesion Count (TLC)

End point title	Percent Change From Baseline in Total Lesion Count (TLC)
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	

<b>End point values</b>	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: Change from Baseline				
arithmetic mean (confidence interval 95%)	-37.0 (-40.9 to -33.2)	-28.4 (-32.3 to -24.6)		

## Statistical analyses

<b>Statistical analysis title</b>	Percent Change from Baseline in TLC at week 12
Statistical analysis description: An ANCOVA was used to compare the percent change from Baseline in TLC in each treatment group at Week 12, with treatment and analysis center as fixed effects and the Baseline TLC as the covariate.	
Comparison groups	CB-03-01 Cream v Vehicle Cream

Number of subjects included in analysis	708
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

### Secondary: Percent Change From Baseline in Non-inflammatory Lesion (NIL) Count

End point title	Percent Change From Baseline in Non-inflammatory Lesion (NIL) Count
End point description: Percent change from Baseline in NIL count in each treatment group at Week 12.	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: % Change from Baseline				
arithmetic mean (confidence interval 95%)	-30.6 (-35.6 to -25.7)	-21.6 (-26.4 to -16.8)		

### Statistical analyses

Statistical analysis title	Percent change from Baseline in NILC at week12
Statistical analysis description: An ANCOVA 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.	
Comparison groups	CB-03-01 Cream v Vehicle Cream
Number of subjects included in analysis	708
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	

<b>End point values</b>	CB-03-01 Cream	Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	353	355		
Units: % Change from Baseline				
arithmetic mean (confidence interval 95%)	-44.8 (-49.0 to -40.5)	-36.5 (-40.8 to -32.2)		

## Statistical analyses

<b>Statistical analysis title</b>	Percent change from Baseline in ILC at week 12
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Statistical analysis description:

An ANCOVA 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.

Comparison groups	CB-03-01 Cream v Vehicle Cream
Number of subjects included in analysis	708
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:

The Safety population was used for all analyses which comprised of all participants enrolled in the study and applied at least one dose of the test article.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

### Reporting groups

Reporting group title	CB-03-01 Cream
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Reporting group description: -

Reporting group title	Vehicle Cream
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Reporting group description: -

Serious adverse events	CB-03-01 Cream	Vehicle Cream	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 353 (0.00%)	1 / 355 (0.28%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 353 (0.00%)	1 / 355 (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: 0.6 %

Non-serious adverse events	CB-03-01 Cream	Vehicle Cream	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 353 (2.55%)	18 / 355 (5.07%)	
Injury, poisoning and procedural complications			
Application site pruritus			

subjects affected / exposed occurrences (all)	2 / 353 (0.57%) 2	3 / 355 (0.85%) 3	
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all)	1 / 353 (0.28%) 1	3 / 355 (0.85%) 4	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 353 (1.70%) 7	12 / 355 (3.38%) 12	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported