Clinical trial results:
An Open Label Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Cortexolone 17-Propionate (CB-03-01) Cream Applied Every 12 Hours for Two Weeks in Subjects with Acne Vulgaris

Summary

EudraCT number	2023-000462-33
Trial protocol	Outside EU/EEA
Global end of trial date	11 November 2013

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	171-7151-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01831960
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Intrepid Therapeutics Inc.
Sponsor organisation address	12463 Rancho Bernardo Road, #537, San Diego, United States, CA 92128-2143
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)	EMEA-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	08 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 November 2013
Global end of trial reached?	Yes
Global end of trial date	11 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to determine a) the adrenal suppression potential and b) the pharmacokinetic (PK) properties of CB-03-01 Cream, 1% in subjects with acne vulgaris

Protection of trial subjects:

Approval on the conduct of the trial was obtained by an IRB and by the FDA prior to study initiation. The study protocol, consent/assent form, participant recruitment materials/process, and other relevant documents were submitted for approval 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 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	07 May 2013
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: 42
Worldwide total number of subjects	42
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)	0
Adolescents (12-17 years)	22

Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

57 subjects were screened for the study; 42 subjects (20 adults in Cohort 1 and 22 adolescents in Cohort 2) were enrolled into the study; 15 subjects were screen failures.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cortexolone 17α-Propionate (Cohort 1)

Arm description:

Cohort 1 enrolled adult subjects.

Arm type	Experimental
Investigational medicinal product name	Cortexolone 17α-Propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Topical cream, 1.0% concentration, applied every twelve hours.

Arm title	Cortexolone 17α-Propionate (Cohort 2)

Arm description:

Cohort 2 enrolled adolescent subjects 12 to less than 18 years of age.

Arm type	Experimental
Investigational medicinal product name	Cortexolone 17α-Propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Topical cream, 1.0% concentration, applied every twelve hours.

Number of subjects in period 1	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)
Started	20	22
Completed	20	22

Baseline characteristics

Reporting groups	
Reporting group title	Cortexolone 17α-Propionate (Cohort 1)
Reporting group description: Cohort 1 enrolled adult subjects.	
Reporting group title	Cortexolone 17α-Propionate (Cohort 2)
Reporting group description: Cohort 2 enrolled adolescent subjects 12 to less than 18 years of age.	

Reporting group values	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)	Total
Number of subjects	20	22	42
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	24.4	15.6	
standard deviation	± 5.84	± 1.33	-
Gender categorical Units: Subjects			
Female	15	12	27
Male	5	10	15
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	20	21	41
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	17	21	38
More than one race	1	1	2
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Cortexolone 17α-Propionate (Cohort 1)
Reporting group description: Cohort 1 enrolled adult subjects.	
Reporting group title	Cortexolone 17α-Propionate (Cohort 2)
Reporting group description: Cohort 2 enrolled adolescent subjects 12 to less than 18 years of age.	

Primary: Change in HPA Axis Response to Cosyntropin

End point title	Change in HPA Axis Response to Cosyntropin[1]
End point description: Measurement of serum cortisol concentrations after stimulation of the adrenal cortex with cosyntropin injection (Cosyntropin Stimulation Test - CST). Prior to CST, a pre-CST blood sample is taken between 7AM to 9AM. Thirty minutes after CST, a post-CST blood sample is collected. HPA axis suppression is defined as a post-stimulation serum cortisol level ≤ 18 µg/dL at Day 14.	
End point type	Primary
End point timeframe: Baseline and Day 14	

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: All analyses were descriptive. Serum cortisol results were summarized for evaluable subjects. HPA axis responses to CST were dichotomized to normal and abnormal.

End point values	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: mcg/dL				
arithmetic mean (standard deviation)				
Baseline (pre-CST)	17.0 (± 5.98)	16.8 (± 4.71)		
Baseline (post-CST)	27.7 (± 3.43)	24.6 (± 3.12)		
Day 14 (pre-CST)	18.1 (± 7.02)	15.4 (± 3.98)		
Day 14 (post-CST)	26.7 (± 5.56)	22.8 (± 2.99)		

Statistical analyses

No statistical analyses for this end point

Primary: PK Profiles (Cmax) of Cortexolone 17α-propionate

End point title	PK Profiles (Cmax) of Cortexolone 17α-propionate[2]
End point description: Max concentration (Cmax) of cortexolone 17α-propionate in plasma following the first application (i.e., Day 1, 0-12 hours) and last application (i.e., Day 14, 0-12 hours).	
End point type	Primary

End point timeframe:

Baseline and Day 14

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: All analyses were descriptive and of exploratory nature. If p-values or confidence intervals (CI) were presented, they were to be interpreted descriptively.
Non-compartmental analysis was used for estimation of PK parameters.

End point values	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax - Day 1 (ng/mL)	3.23 (± 2.01)	3.58 (± 4.30)		
Cmax - Day 14 (ng/mL)	4.46 (± 3.00)	4.61 (± 4.74)		

Statistical analyses

No statistical analyses for this end point

Primary: PK Profiles (AUC) of Cortexolone 17α-propionate

End point title	PK Profiles (AUC) of Cortexolone 17α-propionate[3]

End point description:

Area under the plasma concentration curve (0-12 hours) of cortexolone 17α-propionate at baseline (i.e., Day 1, after first application [0-12 hours]) and at Day 14 (i.e., Day 14, after last application [0-12 hours]).

End point type	Primary

End point timeframe:

Baseline and Day 14

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: All analyses were descriptive and of exploratory nature. If p-values or confidence intervals (CI) were presented, they were to be interpreted descriptively.
Non-compartmental analysis was used for estimation of PK parameters.

End point values	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
AUC_T - Day 1	22.02 (± 13.67)	22.55 (± 22.57)		
AUC_T - Day 14	37.14 (± 22.92)	30.97 (± 24.65)		

Statistical analyses

No statistical analyses for this end point

Primary: PK Profiles (Cavg) of Cortexolone 17α-propionate

End point title	PK Profiles (Cavg) of Cortexolone 17α-propionate[4]

End point description:

Average concentration of cortexolone 17α-propionate in plasma calculated as the ratio of the AUC(0-12 hours) and the dosing interval (i.e., 12 hours) at baseline (i.e., Day 1, after first application) and at Day 14 (after last application).

End point type	Primary

End point timeframe:

Baseline and Day 14

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: All analyses were descriptive and of exploratory nature. If p-values or confidence intervals (CI) were presented, they were to be interpreted descriptively.
Non-compartmental analysis was used for estimation of PK parameters.

End point values	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cavg - Day 1	1.84 (± 1.14)	1.88 (± 1.88)		
Cavg - Day 14	3.10 (± 1.91)	2.58 (± 2.05)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14 days

Adverse event reporting additional description:

Any treatment emergent AEs ongoing at the end of the treatment period (Day 14) were followed until they resolve, the condition stabilizes, the events are otherwise explained, or the subject is lost to follow-up. In addition, all SAEs were followed until resolution as previously stated for study product-related AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Cortexolone 17α-Propionate (Cohort 1)
Reporting group description: -	
Reporting group title	Cortexolone 17α-Propionate (Cohort 2)

Reporting group description: -

Serious adverse events	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cortexolone 17α-Propionate (Cohort 1)	Cortexolone 17α-Propionate (Cohort 2)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 20 (25.00%)	3 / 22 (13.64%)	
Investigations			
ACTH stimulation test abnormal			
subjects affected / exposed	1 / 20 (5.00%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Application site folliculitis			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 22 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1	 0 / 22 (0.00%) 0	
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1	 0 / 22 (0.00%) 0	
Infections and infestations Ear infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1	 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2013	Protocol Amendment #1
11 June 2013	Protocol Amendment #2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported