



Clinical trial results:

An Open Label Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Cortisolone 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) | 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 | 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 17a-Propionate (Cohort 1) |

Arm description:

Cohort 1 enrolled adult subjects.

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cortexolone 17a-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 17a-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 17a-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 17a-Propionate (Cohort 1) | Cortexolone 17a-Propionate (Cohort 2) |
|---------------------------------------|---------------------------------------|---------------------------------------|
| Started | 20 | 22 |
| Completed | 20 | 22 |

Baseline characteristics

Reporting groups

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

| Reporting group values | Cortexolone 17a-Propionate (Cohort 1) | Cortexolone 17a-Propionate (Cohort 2) | Total |
|------------------------------------|---------------------------------------|---------------------------------------|-------|
| Number of subjects | 20 | 22 | 42 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 24.4 ± 5.84 | 15.6 ± 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 17 α -Propionate (Cohort 1) |
| Reporting group description: Cohort 1 enrolled adult subjects. | |
| Reporting group title | Cortexolone 17 α -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 μ g/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 17 α -Propionate (Cohort 1) | Cortexolone 17 α -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 (\pm 5.98) | 16.8 (\pm 4.71) | | |
| Baseline (post-CST) | 27.7 (\pm 3.43) | 24.6 (\pm 3.12) | | |
| Day 14 (pre-CST) | 18.1 (\pm 7.02) | 15.4 (\pm 3.98) | | |
| Day 14 (post-CST) | 26.7 (\pm 5.56) | 22.8 (\pm 2.99) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|--|
| End point title | PK Profiles (Cmax) of Cortexolone 17 α -propionate ^[2] |
| End point description: Max concentration (Cmax) of cortexolone 17 α -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 | Cortisolone 17 α -Propionate (Cohort 1) | Cortisolone 17 α -Propionate (Cohort 2) | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 22 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| C _{max} - Day 1 (ng/mL) | 3.23 (\pm 2.01) | 3.58 (\pm 4.30) | | |
| C _{max} - Day 14 (ng/mL) | 4.46 (\pm 3.00) | 4.61 (\pm 4.74) | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Area under the plasma concentration curve (0-12 hours) of cortisolone 17 α -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 | Cortisolone 17 α -Propionate (Cohort 1) | Cortisolone 17 α -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 (\pm 13.67) | 22.55 (\pm 22.57) | | |
| AUC _T - Day 14 | 37.14 (\pm 22.92) | 30.97 (\pm 24.65) | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Average concentration of cortexolone 17 α -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 17 α -Propionate (Cohort 1) | Cortexolone 17 α -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 (\pm 1.14) | 1.88 (\pm 1.88) | | |
| Cavg - Day 14 | 3.10 (\pm 1.91) | 2.58 (\pm 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

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

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Cortexolone 17a-Propionate (Cohort 1) |
|-----------------------|---------------------------------------|

Reporting group description: -

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Cortexolone 17a-Propionate (Cohort 2) |
|-----------------------|---------------------------------------|

Reporting group description: -

| Serious adverse events | Cortexolone 17a-Propionate (Cohort 1) | Cortexolone 17a-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 17a-Propionate (Cohort 1) | Cortexolone 17a-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) | 0 / 20 (0.00%) 0 | 1 / 22 (4.55%) 1 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 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