



Clinical trial results:

An open label evaluation of the adrenal suppression potential and pharmacokinetic properties of twice daily halobetasol propionate foam, 0.05% in subjects 12 to less than 18 years of age with plaque psoriasis receiving two weeks of treatment

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2018-003845-40 |
| Trial protocol | PL |
| Global end of trial date | 30 December 2019 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 05 September 2020 |
| First version publication date | 05 September 2020 |
| Summary attachment (see zip file) | 122-0551-209_CSR synopsis_20200220 (122-0551-209_CSR synopsis.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | 122-0551-209 |
|-----------------------|--------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Mayne Pharma LLC |
| Sponsor organisation address | 3301 Benson Drive, Suite 401, Raleigh, United States, NC 27609 |
| Public contact | Clinical Project Manager, Therapeutics, Inc., 001 858571-1800, gliu@therapeuticsinc.com |
| Scientific contact | Clinical Project Manager, Therapeutics, Inc., 001 858571-1800, gliu@therapeuticsinc.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 | 26 February 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 December 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to determine the adrenal suppression potential and the pharmacokinetic (PK) properties of HBP Foam, 0.05% applied twice daily in subjects who are 12 to less than 18 years of age with stable plaque psoriasis.

Protection of trial subjects:

The study protocol, consent/assent form, participant recruitment materials/process and other relevant study documents were submitted to involved Ethic Committee (ECs)/Institutional Review Boards (IRBs) and approved prior to study initiation.

This study was conducted in accordance with principles of the Declaration of Helsinki, with the current Good Clinical Practice guidelines and with other applicable regulations. The investigators and all study staff conducted the study in compliance with the study protocol.

Interested individuals, male and female subjects 12 to 17 years of age, accompanied by their parent or legal guardian were given an opportunity to discuss the activities involved in study participation with the site staff and the principal investigator. An IRB/EC-approved informed consent/assent form and subject instruction sheet was given to the potential subject and his/her parent or legal guardian and an opportunity afforded to read the consent/assent form and ask questions. Those individuals interested in participation were requested to sign the informed consent/assent form prior to the performance of any study-related procedures. The rights, safety and wellbeing of the study subjects were the most important considerations and prevailed over the interests of science and society. Identifying any untoward medical occurrence and timely and complete reporting of all AEs was aimed at the most efficient protection of the safety of study subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 February 2019 |
| 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: 6 |
| Country: Number of subjects enrolled | Ukraine: 11 |
| Country: Number of subjects enrolled | Georgia: 1 |
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 6 |

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) | 24 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Enrollment goal was 25 subjects to get at least 20 evaluable subjects; 24 subjects were enrolled and 24 subjects analysed.

Study Period (Years): < 1 year

June 14, 2019 (date of first subject enrolled)

December 30, 2019 (date of last subject completed)

Territories: Georgia, Poland, Ukraine, USA

Pre-assignment

Screening details:

34 subjects were screened; 10 subjects were screen failure. 9 subjects met excl. cr. #17 (a screening CST with a post 30-minute stimulation cortisol level of ≤ 18 µg/dL), 1 subject met excl. cr. #1 (spontaneously improving/rapidly deteriorating plaque psoriasis) and failed to meet incl. cr. #3 (had a clinical diagnosis of stable PP min 10% BSA)

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 24 |
| Number of subjects completed | 24 |

Period 1

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

Arms

| | |
|-----------|---|
| Arm title | Treatment with Halobetasol Propionate (HBP) Foam, 0.05% |
|-----------|---|

Arm description:

All subjects enrolled in the study who were dispensed and applied HBP at least once were included in the analysis of safety and were considered the Safety population. Subjects applied the initial dose of HBP in the clinic on Day 1. The Evaluable population included those subjects in the Safety population who had both Screening and EOS serum cortisol data (pre- and post-cosyntropin stimulation) and met all specified criteria by protocol. Subjects included in the pharmacokinetic analysis (PK population) included those subjects who did not have any significant protocol deviations and must have had at least an 80% – 120% dose compliance based on number of applications.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Halobetasol Propionate (HBP) Foam, 0.05% |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cutaneous foam |
| Routes of administration | Topical use |

Dosage and administration details:

All subjects received HBP Foam, 0.05% in an open label manner. Subjects were instructed to apply a maximum of approximately 50 grams weekly of the test article (HBP Foam) to affected areas designated by the investigator, twice daily (approximately every 12 hours) for up to 2 weeks.

| Number of subjects in period 1 | Treatment with Halobetasol Propionate (HBP) Foam, 0.05% |
|---------------------------------------|--|
| Started | 24 |
| Completed | 24 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|--|---------------|-------|--|
| Number of subjects | 24 | 24 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 24 | 24 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 14.7 | | |
| standard deviation | ± 1.76 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 11 | |
| Male | 13 | 13 | |

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety population included all subjects enrolled in the study who were dispensed and applied test article at least once. All enrolled subjects (N=24) were included in the analysis of safety).

| | |
|----------------------------|----------------------|
| Subject analysis set title | Evaluable population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Evaluable population (N=23) included those subjects in the Safety population who had both Screening and EOS serum cortisol data (pre- and post-cosyntropin stimulation) and met the following criteria:

- Met all inclusion/exclusion criteria, including normal response to cosyntropin stimulation defined as a Screening CST with a 30-minute post-stimulation cortisol level of > 18 µg/dL.
- Screening and EOS CST were conducted between 7AM–9AM.
- EOS CST was conducted within ±1 hour of the Screening CST.
- Applied at least 80% and no more than 120% of the expected number of applications and applied the final dose no more than 14 hours prior to the start of the CST.
- Had not taken or applied any medications that may have interfered with HPA axis function.
- Did not have any other significant protocol deviations.

There was 1 enrolled subject who was excluded from the Evaluable population for using a prohibited

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Pharmacokinetic population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PK population (N=23) included those subjects who did not have had any significant protocol deviations and had at least an 80% – 120% dose compliance based on number of applications. There was 1 enrolled subject who was excluded from the PK population for using a prohibited medication.

| Reporting group values | Safety Population | Evaluable population | Pharmacokinetic population |
|--|-------------------|----------------------|----------------------------|
| Number of subjects | 24 | 23 | 23 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 24 | 23 | 23 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 14.7 | 14.8 | 14.8 |
| standard deviation | ± 1.76 | ± 1.79 | ± 1.79 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 10 | 10 |
| Male | 13 | 13 | 13 |

End points

End points reporting groups

| | |
|-----------------------|---|
| Reporting group title | Treatment with Halobetasol Propionate (HBP) Foam, 0.05% |
|-----------------------|---|

Reporting group description:

All subjects enrolled in the study who were dispensed and applied HBP at least once were included in the analysis of safety and were considered the Safety population. Subjects applied the initial dose of HBP in the clinic on Day 1. The Evaluable population included those subjects in the Safety population who had both Screening and EOS serum cortisol data (pre- and post-cosyntropin stimulation) and met all specified criteria by protocol. Subjects included in the pharmacokinetic analysis (PK population) included those subjects who did not have any significant protocol deviations and must have had at least an 80% – 120% dose compliance based on number of applications.

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety population included all subjects enrolled in the study who were dispensed and applied test article at least once. All enrolled subjects (N=24) were included in the analysis of safety).

| | |
|----------------------------|----------------------|
| Subject analysis set title | Evaluable population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Evaluable population (N=23) included those subjects in the Safety population who had both Screening and EOS serum cortisol data (pre- and post-cosyntropin stimulation) and met the following criteria:

- Met all inclusion/exclusion criteria, including normal response to cosyntropin stimulation defined as a Screening CST with a 30-minute post-stimulation cortisol level of > 18 µg/dL.
- Screening and EOS CST were conducted between 7AM–9AM.
- EOS CST was conducted within ±1 hour of the Screening CST.
- Applied at least 80% and no more than 120% of the expected number of applications and applied the final dose no more than 14 hours prior to the start of the CST.
- Had not taken or applied any medications that may have interfered with HPA axis function.
- Did not have any other significant protocol deviations.

There was 1 enrolled subject who was excluded from the Evaluable population for using a prohibited medication

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Pharmacokinetic population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PK population (N=23) included those subjects who did not have had any significant protocol deviations and had at least an 80% – 120% dose compliance based on number of applications. There was 1 enrolled subject who was excluded from the PK population for using a prohibited medication.

Primary: HPA Axis Suppression

| | |
|-----------------|-------------------------------------|
| End point title | HPA Axis Suppression ^[1] |
|-----------------|-------------------------------------|

End point description:

Hypothalamic-pituitary-adrenal (HPA) axis responses to stimulation by cosyntropin were dichotomized to “normal” and “abnormal”. An abnormal HPA axis response was defined as a 30-minute post-stimulation serum cortisol level that was ≤18 µg/dL at the end of study (EOS).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

End of study

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: The proportion of subjects manifesting laboratory based evidence of adrenal suppression at EOS is presented along with 95% confidence intervals for the Evaluable and Safety populations.

Descriptive statistics for the daily dose of test article are tabulated separately for suppressed and non-suppressed subjects.

| End point values | Safety Population | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: numbers | | | | |
| Abnormal Cortisol $\leq 18 \mu\text{g/dL}$ | 6 | | | |
| Normal (Cortisol $> 18 \mu\text{g/dL}$) | 18 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Levels of Halobetasol Propionate

| | |
|------------------------|--|
| End point title | Plasma Levels of Halobetasol Propionate ^[2] |
| End point description: | Plasma Trough Concentrations of Halobetasol Propionate (PK) at screening, day 8 and EOS (Day 15) |
| End point type | Primary |
| End point timeframe: | At Screening, Day 8, and Day 15/EOS approximately 12 hour post-treatment |

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: Morning trough concentrations of HBP in plasma at Screening, Day 8, and Day 15 is summarized for the PK population using geometric mean, coefficient of variation in addition to n, mean, median, standard deviation, minimum and maximum.

| End point values | Pharmacokinetic population | | | |
|--------------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 23 | | | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| screening (Day0) | 0 (\pm 0) | | | |
| Day 8 | 154.6 (\pm 308.6) | | | |
| EOS (Day15) | 59.9 (\pm 90.15) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's global assessment (IGA)

| | |
|-----------------|--|
| End point title | Investigator's global assessment (IGA) |
|-----------------|--|

End point description:

The IGA score (5-point scale of 0 to 4) is an evaluation of the overall severity of a subject's psoriasis in the Treatment Area and takes into consideration the three individual characteristics of psoriasis (plaque elevation, scaling, and erythema). At Screening, Baseline Visit/Day 1, Day 8, and Day 15/EOS, the investigator will evaluate all active psoriasis plaques that are in the Treatment Area and report the single integer score that describes the overall severity of the subject's psoriasis using the predefined scale (0-clear; 1-almost clear; 2-mild; 3-moderate; 4-severe).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Screening, Baseline Visit/Day 1, Day 8, and Day 15/EOS, the investigator will evaluate all active psoriasis plaques that are in the Treatment Area

| End point values | Evaluable population | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | | | | |
| Units: number | | | | |
| screening (0) | 0 | | | |
| screening (1) | 0 | | | |
| screening (2) | 0 | | | |
| screening (3) | 21 | | | |
| screening (4) | 2 | | | |
| Day 8 (0) | 1 | | | |
| Day8 (1) | 3 | | | |
| Day 8 (2) | 10 | | | |
| Day8 (3) | 9 | | | |
| Day 8 (4) | 0 | | | |
| EOS Day15 (0) | 5 | | | |
| EOS Day 15 (1) | 10 | | | |
| EOS Day 15(2) | 5 | | | |
| EOS Day 15 (3) | 2 | | | |
| EOS Day 15 (4) | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Body Surface Area Treated with Test Article

| | |
|-----------------|---|
| End point title | Percent Body Surface Area Treated with Test Article |
|-----------------|---|

End point description:

This is defined as the BSA which is affected with psoriasis within the Treatment Area that will be treated. In most cases there is no difference between Percent BSA Affected and Percent BSA Treated unless the affected BSA is too large to be treated with the drug dosing limitation of 50 grams per week (e.g., 3.5 grams per application).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

The Percent BSA to be Treated will be estimated at Baseline/Day 1 and Day 8

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Evaluable population | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 23 | | | |
| Units: percentage | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 14.5 (± 3.81) | | | |
| Day 8 | 12.6 (± 5.2) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening to EoS (Day15)

Adverse event reporting additional description:

An AE was any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. All local skin reactions (LSR) were assessed pre-application and only burning/stinging were assessed post-application. There were no subjects who had an LSR that worsened during the study.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Safety population |
|-----------------------|-------------------|

Reporting group description:

The study involved 1 arm, thus all study participants are considered as one group.

| Serious adverse events | Safety population | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Safety population | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 24 (29.17%) | | |
| Investigations | | | |
| ACTH stimulation test abnormal | Additional description: Laboratory based evidence of abnormal HPA axis response at Day 15/EOS as documented by a 30-minute post-stimulation serum cortisol level of ≤ 18 µg/dL. All "suppressed" subjects returned to normal HBP axis function (as assessed by CST) at their initial visit. | | |
| subjects affected / exposed | 6 / 24 (25.00%) | | |
| occurrences (all) | 6 | | |
| Red blood cells urine positive | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 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