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

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.

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 <=18 µg/dL)	6			
Normal (Cortisol >18 µg/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 (± 0)			
Day 8	154.6 (± 308.6)			
EOS (Day15)	59.9 (± 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 Day 8	14.5 (± 3.81) 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 initia		
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 occurrences (all)	 1 / 24 (4.17%) 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