Clinical trial results:
Safety and Effect of LEO 90100 aerosol foam on the HPA Axis and Calcium Metabolism in Adolescent Subjects (Aged 12 to < 17 Years) with Plaque Psoriasis

A phase 2 trial evaluating the safety and efficacy of once daily topical treatment with LEO 90100 aerosol foam in adolescent subjects with plaque psoriasis

An international, multi-centre, prospective, open-label, non-controlled, single-group, 4-week trial in adolescent subjects with plaque psoriasis

Summary

EudraCT number	2015-000839-33
Trial protocol	NL PL
Global end of trial date	28 March 2018
Results information	
Result version number	v4 (current)
This version publication date	30 January 2019
First version publication date	14 October 2018
Version creation reason	• Correction of full data set Change made to the endpoint description for Change in Itch as Assessed on a Visual Analog Scale (VAS) From Baseline to Week 4 to align with comments received from clinicaltrials.gov.

Trial information

Trial identification	
Sponsor protocol code	LP0053-1108
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02387853
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	LEO Pharma A/S
Sponsor organisation address	Industriparken 55, Ballerup, Denmark, 2750
Public contact	Clinical Disclosure Specialist, LEO Pharma A/S, +45 44945888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure Specialist, LEO Pharma A/S, +45 44945888,

disclosure@leo-pharma.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	22 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 March 2018
Global end of trial reached?	Yes
Global end of trial date	28 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the safety of once daily use of LEO 90100 in adolescent subjects (aged 12 to < 17 years) with plaque psoriasis on the body and scalp.

Protection of trial subjects:

This clinical trial was conducted in accordance with the revision current at the start of the trial of the World Medical Association’s Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. All subjects received written and verbal information concerning the clinical trial. This information emphasised that participation in the clinical trial was voluntary and that the subject could withdraw from the clinical trial at any time and for any reason. All subjects and their legally acceptable representatives were given an opportunity to ask questions and were given sufficient time to consider before consenting. Subjects who were not of legal age gave assent to their participation in the trial. The subject’s and legally acceptable representatives' signed and dated informed consent and assent to participate in the clinical trial were obtained prior to any trial related activities being carried out in accordance with ICH Good Clinical Practice (GCP) Section 4.8 and all applicable laws and regulations.
Overdosage with calcipotriol may be associated with hypercalcaemia, and clinically important hypercalcaemia could be managed at the investigator’s discretion with rehydration, biphosphonate administration or according to local instructions.
Overdosage with betamethasone dipropionate may result in suppression of the pituitary adrenal function, and could be treated symptomatically at the investigator's discretion.
There is a risk of allergic hypersensitivity reactions with administration of Cortrosyn®/Synacthen®. Prior to the injection of Cortrosyn®/Synacthen®, the physician administering the injection was prepared to treat any possible hypersensitivity reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 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	Netherlands: 9
Country: Number of subjects enrolled	Poland: 71
Country: Number of subjects enrolled	Romania: 34
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	117
EEA total number of subjects	114

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)	117
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male/female 12-17 years, psoriasis on body and scalp
Subj. not performing HPA axis test: Plaque psoriasis ≥2% BSA, ≥10% of scalp, ≥ mild severity
Subj. performing HPA axis test: Plaque psoriasis ≥10% BSA, ≥20% of scalp, ≥ moderate severity, normal HPA-axis function
117 screened. 106 assigned to treatment, 8 screening failures, 3 withdrew consent

Period 1

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

Arms

Arm title	LEO 90100

Arm description:

This arm contains all 106 subjects that were assigned to treatment and constitutes the full analysis set and the safety analysis set. 33 subjects in this arm performed additional baseline and post-baseline HPA axis assessments and constitute the per protocol analysis set.

Arm type	Experimental
Investigational medicinal product name	LEO 90100
Investigational medicinal product code	
Other name	Enstilar®
Pharmaceutical forms	Cutaneous foam
Routes of administration	Topical use

Dosage and administration details:

LEO 90100 is formulated as an aerosol foam formulation containing calcipotriol 50 mcg/g (as hydrate) and betamethasone 0.5 mg/g (as dipropionate). LEO 90100 was applied once daily to body and scalp psoriasis lesions. Subjects in the HPA axis cohort were to continue the treatment, even if their lesions had cleared at Week 2. Subjects in the non-HPA axis cohort were allowed to discontinue treatment if the psoriasis lesions had cleared at Week 2 (according to the investigator), but should stay in the trial. During periods of discontinuation of treatment, those cleared subjects were to restart treatment if the psoriasis re-appeared.

Number of subjects in period 1[1]	LEO 90100
Started	106
Completed	103
Not completed	3
Consent withdrawn by subject	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number of enrolled subjects include all subjects who provided consent for participation in the trial and were screened. Out of the 117 subjects who were screened, 106 subjects met all inclusion criteria and none of the exclusion criteria, and were assigned to treatment. These 106

subjects are subjects are included in the data for the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	106	106	
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)	106	106	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	14.2		
standard deviation	± 1.4	-	
Gender categorical Units: Subjects			
Female	61	61	
Male	45	45	

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects assigned to treatment are included in the full analysis set and were analysed for efficacy. 106 subjects were assigned to the treatment. Thus the full analysis set consists of 106 subjects.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set is defined by excluding subjects from the full analysis set who either received no treatment with the IMP and/or for whom no post-baseline safety evaluations are available. 106 subjects were assigned to treatment and had safety information collected. For 1 subject it was unknown whether any IMP was applied, but since it could neither be confirmed nor denied that the subject did not apply IMP, this subject was included in the safety analysis set. Therefore, the safety analysis set comprised 106 subjects.

The analysis of the results from the ACTH-challenge test is based on the per protocol analysis set and not on the safety analysis set.

Subject analysis set title	Per protocol analysis set
Subject analysis set type	Per protocol

Subject analysis set description:

For the analysis of the results from the ACTH-challenge test, a per protocol analysis set was defined by including subjects undergoing HPA axis assessments from the full analysis set, however excluding the subjects who:
• Received no treatment with the IMP
• Provided no results for the ACTH-challenge test at Week 4
• And/or do not fulfil inclusion criterion 17 concerning evidence of normal adrenal function at baseline: Normal HPA axis function at SV2 (serum cortisol concentration above 5 mcg/dl before ACTH challenge and serum cortisol concentration above 18 mcg/dl 30 minutes after ACTH challenge).
A total of 34 subjects in the full analysis set were assigned to perform the ACTH challenge test. 33 subjects provided data for the ACTH-challenge, thus the per protocol analysis set comprises 33 subjects.

Subject analysis set title	24-hour urine HPA set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

24-hour urine samples were only collected from subjects in the HPA axis cohort. All 34 subjects in the HPA axis cohort were included in this analysis set, referred to as the '24-hour urine HPA set'.

Subject analysis set title	Spot urine non-HPA set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Some analytes in the spot urine samples (calcium, phosphate, and creatinine) were only to be measured in subjects in the non-HPA axis cohort. This analysis set is called 'spot urine non-HPA set' and comprised 72 subjects.

Reporting group values	Full analysis set	Safety analysis set	Per protocol analysis set
Number of subjects	106	106	33
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)	106	106	33
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	14.2	14.2	14.2
standard deviation	± 1.4	± 1.4	± 1.3
Gender categorical Units: Subjects			
Female	61	61	16
Male	45	45	17

Reporting group values	24-hour urine HPA set	Spot urine non-HPA set	
Number of subjects	34	72	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	±	±	
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	LEO 90100

Reporting group description:

This arm contains all 106 subjects that were assigned to treatment and constitutes the full analysis set and the safety analysis set. 33 subjects in this arm performed additional baseline and post-baseline HPA axis assessments and constitute the per protocol analysis set.

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects assigned to treatment are included in the full analysis set and were analysed for efficacy. 106 subjects were assigned to the treatment. Thus the full analysis set consists of 106 subjects.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set is defined by excluding subjects from the full analysis set who either received no treatment with the IMP and/or for whom no post-baseline safety evaluations are available. 106 subjects were assigned to treatment and had safety information collected. For 1 subject it was unknown whether any IMP was applied, but since it could neither be confirmed nor denied that the subject did not apply IMP, this subject was included in the safety analysis set. Therefore, the safety analysis set comprised 106 subjects.

The analysis of the results from the ACTH-challenge test is based on the per protocol analysis set and not on the safety analysis set.

Subject analysis set title	Per protocol analysis set
Subject analysis set type	Per protocol

Subject analysis set description:

For the analysis of the results from the ACTH-challenge test, a per protocol analysis set was defined by including subjects undergoing HPA axis assessments from the full analysis set, however excluding the subjects who:
• Received no treatment with the IMP
• Provided no results for the ACTH-challenge test at Week 4
• And/or do not fulfil inclusion criterion 17 concerning evidence of normal adrenal function at baseline: Normal HPA axis function at SV2 (serum cortisol concentration above 5 mcg/dl before ACTH challenge and serum cortisol concentration above 18 mcg/dl 30 minutes after ACTH challenge).
A total of 34 subjects in the full analysis set were assigned to perform the ACTH challenge test. 33 subjects provided data for the ACTH-challenge, thus the per protocol analysis set comprises 33 subjects.

Subject analysis set title	24-hour urine HPA set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

24-hour urine samples were only collected from subjects in the HPA axis cohort. All 34 subjects in the HPA axis cohort were included in this analysis set, referred to as the ‘24-hour urine HPA set’.

Subject analysis set title	Spot urine non-HPA set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Some analytes in the spot urine samples (calcium, phosphate, and creatinine) were only to be measured in subjects in the non-HPA axis cohort. This analysis set is called ‘spot urine non-HPA set’ and comprised 72 subjects.

Primary: Number of Subjects with Adverse Events (AEs)

End point title	Number of Subjects with Adverse Events (AEs)[1]

End point description:

Number of adverse events in the safety analysis set, defined by excluding subjects from the full analysis set who either received no treatment with the IMP and/or for whom no post-baseline safety evaluations are available.

End point type	Primary

End point timeframe:

From Week -1 to Week 8

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: No statistical analysis is required for this end point.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: Number of subjects				
Upper respiratory tract infection	8			
Nasopharyngitis	4			
Folliculitis	1			
Impetigo	1			
Oral herpes	1			
Pharyngitis	1			
Pulpitis dental	1			
Rhinitis	1			
Acne	2			
Erythema	1			
Pruritus generalised	1			
Psoriasis	1			
Skin reaction	1			
Application site pain	1			
Product physical consistency issue	1			
Arthralgia	1			
Myalgia	1			
Myopia	1			
Arthropod bite	1			
Haemangioma of liver	1			
Skin neoplasm excision	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with serum cortisol concentration of ≤18 mcg/dl at 30 minutes after ACTH-challenge at Week 4

End point title	Number of Subjects with serum cortisol concentration of ≤18 mcg/dl at 30 minutes after ACTH-challenge at Week 4[2]

End point description:

Number of subjects with serum cortisol concentration of ≤18 mcg/dl at 30 minutes after ACTH-challenge at Week 4 in the per protocol analysis set, defined as all subjects from the full analysis set who were in the HPA axis cohort but excluding subjects who did not receive any treatment with the IMP, did not provide any results for the HPA axis test at Week 4, or did not meet the inclusion criterion concerning evidence of normal adrenal function at baseline.

End point type	Primary

End point timeframe:

30 minutes after ACTH-challenge at Week 4

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: No statistical analysis is required for this end point.

End point values	Per protocol analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Number of subjects				
Serum cortisol equal to or below 18 mcg/dl	3			
Serum cortisol above 18 mcg/dl	30			

Statistical analyses

No statistical analyses for this end point

Primary: Change in albumin-corrected serum calcium from baseline to Week 4

End point title	Change in albumin-corrected serum calcium from baseline to Week 4[3]

End point description:

Change in albumin-corrected serum calcium from baseline to Week 4 in safety analysis set, defined by excluding subjects from the full analysis set who either received no treatment with the IMP and/or for whom no post-baseline safety evaluations are available.

End point type	Primary

End point timeframe:

From baseline to Week 4

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: No statistical analysis is required for this end point.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	101			
Units: mmol/L				
arithmetic mean (standard deviation)	-0.016 (± 0.119)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in calcium excretion in 24-hour urine from baseline to Week 4

End point title	Change in calcium excretion in 24-hour urine from baseline to Week 4[4]

End point description:

Change in calcium excretion in 24-hour urine collection from baseline to Week 4 in the 24-hour urine

HPA set, defined as all subjects in the safety analysis set who underwent HPA-axis testing.

End point type	Primary

End point timeframe:

From baseline to Week 4

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: No statistical analysis is required for this end point.

End point values	24-hour urine HPA set			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: mmol/24hr				
arithmetic mean (standard deviation)	-0.335 (± 2.076)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in calcium:creatinine ratio in 24-hour urine from baseline to Week 4

End point title	Change in calcium:creatinine ratio in 24-hour urine from baseline to Week 4[5]

End point description:

Change in calcium:creatinine ratio in 24-hour urine collection from baseline to Week 4 in the 24-hour urine in HPA set, defined as all subjects in the safety analysis set who underwent HPA-axis testing.

End point type	Primary

End point timeframe:

From baseline to Week 4

Notes:

[5] - 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: No statistical analysis is required for this end point.

End point values	24-hour urine HPA set			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: mmol/g				
arithmetic mean (standard deviation)	-0.2892 (± 2.1185)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with serum cortisol concentration ≤18 mcg/dL at both 30 and 60 minutes after ACTH-challenge at Week 4

End point title	Number of Subjects with serum cortisol concentration ≤18 mcg/dL at both 30 and 60 minutes after ACTH-challenge at Week 4

End point description:

Number of subjects with serum cortisol concentration ≤18 mcg/dL at both 30 and 60 minutes after ACTH-challenge at Week 4 in the per protocol analysis set, defined as all subjects from the full analysis set who were in the HPA axis cohort but excluding subjects who did not receive any treatment with the IMP, did not provide any results for the HPA axis test at Week 4, or did not meet the inclusion criterion concerning evidence of adrenal function at baseline.

End point type	Secondary

End point timeframe:

30 and 60 minutes after ACTH-challenge at Week 4

End point values	Per protocol analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Number of subjects				
Serum cortisol equal to or below 18 mcg/dL	1			
Serum cortisol above 18 mcg/dl	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in calcium:creatinine ratio in spot urine samples from baseline to Week 4

End point title	Change in calcium:creatinine ratio in spot urine samples from baseline to Week 4

End point description:

Change in calcium:creatinine ratio in spot urine samples from baseline to Week 4 in the spot urine non-HPA set, defined as all subjects in the safety analysis set who did not undergo HPA-axis testing.

End point type	Secondary

End point timeframe:

From baseline to Week 4

End point values	Spot urine non-HPA set			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: mmol/g				
arithmetic mean (standard deviation)	0.4620 (± 1.8892)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with 'treatment success' according to Physician's Global Assessment (PGA) on body

End point title	Number of Subjects with 'treatment success' according to Physician's Global Assessment (PGA) on body

End point description:

Number of subjects with 'treatment success' according to Physician's Global Assessment (PGA) on body in the full analysis set, defined as the 106 subjects assigned to treatment. Treatment success was defined as 'clear' or 'almost clear' for subjects with at least 'moderate' disease at baseline according to the PGA, and defined as 'clear' for subjects with mild disease at baseline according to the PGA.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[6]			
Units: Number of subjects				
Yes	74			
No	29			

Notes:

[6] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with 'treatment success' according to Physician's Global Assessment (PGA) on scalp

End point title	Number of Subjects with 'treatment success' according to Physician's Global Assessment (PGA) on scalp

End point description:

Number of subjects with 'treatment success' according to Physician's Global Assessment (PGA) on Scalp in the full analysis set, defined as the 106 subjects assigned to treatment. Treatment success was defined as 'clear' or 'almost clear' for subjects with at least 'moderate' disease at baseline according to the PGA, and defined as 'clear' for subjects with mild disease at baseline according to the PGA.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[7]			
Units: Number of subjects				
Yes	78			
No	25			

Notes:

[7] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in PASI from baseline to Week 4

End point title	Percentage change in PASI from baseline to Week 4

End point description:

Percentage change in Psoriasis area and severity index (PASI) score from baseline to Week 4. Psoriasis area and severity index (PASI) assesses extent and severity of clinical signs of psoriasis vulgaris. Body surface is divided in 4 ares: head (incl. neck), arms (incl. hands), trunk (incl. flexures) and legs (incl. buttocks and feet). Each area is scored from 0-6 for extent of psoriasis and from 0-4 for redness, thickness, and scaliness, and an area PASI score is calculated. The total PASI score is calculated from each area's score. The PASI score ranges from 0 (clear skin) to 72 (maximum disease), a PASI score higher than 10 generally corresponds to moderate-to-severe disease.

End point type	Secondary

End point timeframe:

From baseline to Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[8]			
Units: Percentage change in PASI				
arithmetic mean (standard deviation)	-82.05 (± 17.87)			

Notes:

[8] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with ‘treatment success’ according to the Subject’s Global Assessment of disease severity on the body at Week 4

End point title	Number of Subjects with ‘treatment success’ according to the Subject’s Global Assessment of disease severity on the body at Week 4

End point description:

Number of subjects with ‘treatment success’ according to the Subject’s Global Assessment of disease severity on the body at Week 4 in the full analysis set, defined as the 106 subjects assigned to treatment. Treatment success was defined as 'clear' or 'very mild' according to the Subject's Global Assessment of disease severity.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[9]			
Units: Number of subjects				
Yes	86			
No	17			

Notes:

[9] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 'treatment success' according to the Subject's Global Assessment of disease severity on the scalp at Week 4

End point title	Number of Subjects With 'treatment success' according to the Subject's Global Assessment of disease severity on the scalp at Week 4

End point description:

Number of subjects with 'treatment success' according to the Subject's Global Assessment of disease severity on the scalp at Week 4 in the full analysis set, defined as the 106 subjects assigned to treatment. Treatment success was defined as 'clear' or 'very mild' according to the Subject's Global Assessment of disease severity.

End point type	Secondary

End point timeframe:

Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[10]			
Units: Number of subjects				
Yes	84			
No	19			

Notes:

[10] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Change in itch as assessed on a visual analog scale (VAS) from baseline

to Week 4

End point title	Change in itch as assessed on a visual analog scale (VAS) from baseline to Week 4

End point description:

Change in itch as assessed on a visual analog scale (VAS) from baseline to Week 4 in the full analysis set, defined as the 106 subjects assigned to treatment. The assessments were made on a 100 mm (100 mm = 10 cm) horizontal VAS anchored at 0 ('no itch at all') and 10 ('worst itch you can imagine'). Subjects were asked to put a vertical line on the scale at the spot he/she felt best reflected the maximal itch intensity during the last 24 hours. The distance from 0 to the subject's indication line was measured in mm, thus higher scores indicated a worse outcome.

End point type	Secondary

End point timeframe:

From baseline to Week 4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	103[11]			
Units: mm on VAS scale				
arithmetic mean (standard deviation)	-32.5 (± 27.3)			

Notes:

[11] - 3 subjects withdrew from the trial prior to Week 4 visit, 103 subjects were included in the analysis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day -28 up to Day 56

Adverse event reporting additional description:

AEs/SAEs were followed up until final outcome was determined. After a subject left the trial, investigator followed up all SAEs and AEs deemed possibly/probably related to IMP for 14± 2 days or until final outcome was determined, whichever came first.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	All subjects

Reporting group description:

This arm contains all 106 subjects that were assigned to treatment and constitutes the safety analysis set.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 106 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 106 (20.75%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Surgical and medical procedures			

Skin neoplasm excision subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1		
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all) Product physical consistency issue subjects affected / exposed occurrences (all)	 1 / 106 (0.94%) 1 1 / 106 (0.94%) 1		
Eye disorders Myopia subjects affected / exposed occurrences (all)	 1 / 106 (0.94%) 1		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Pruritus generalised subjects affected / exposed occurrences (all) Skin reaction subjects affected / exposed occurrences (all)	 2 / 106 (1.89%) 2 1 / 106 (0.94%) 1 1 / 106 (0.94%) 1 1 / 106 (0.94%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 1 / 106 (0.94%) 1 1 / 106 (0.94%) 1		
Infections and infestations			

Upper respiratory tract infection			
subjects affected / exposed	8 / 106 (7.55%)		
occurrences (all)	8		
Nasopharyngitis			
subjects affected / exposed	4 / 106 (3.77%)		
occurrences (all)	4		
Folliculitis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Impetigo			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		
Psoriasis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2015	The amendment was triggered by comments received from the FDA. - Local safety and tolerability assessment was added. - The use of Synacthen® was added (European sites only) - It was specified that subjects in the HPA axis cohort should continue their treatment even if their lesions had cleared at Week 2. - A physical examination was added at Week 4 and at early withdrawal. - Vital signs were added at baseline and Week 2 - Temperature (oral or ear) was added to vital signs. - The PGA scale (Table 12) was updated to also include levels 0 (clear) and 1 (almost clear).
18 January 2016	This amendment was made to correct several minor errors. The following other important changes were made: - It was specified that Synacthen® was provided to the sites in Poland and Romania. - It was specified that cortisol was to be measured at SV2 and Week 4.
14 March 2016	This amendment was made to correct some minor errors.
29 August 2016	This amendment was made to correct an error, namely that serum cortisol analysis was mandated for all subjects. This measurement was only required for subjects in the HPA axis cohort. The following other important changes were made: - A separate schedule of trial procedures was added for subjects in the non-HPA axis cohort. - It was specified that LEO 90100 has different storage conditions in EU and the US (according to approved label).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported