Clinical trial results:
Efficacy of twice daily application of LEO 124249 ointment 30 mg/g for 12 weeks on eyebrow alopecia areata. Exploratory Phase 2a

Summary

EudraCT number	2017-002720-24
Trial protocol	DK
Global end of trial date	16 May 2018

Results information

Result version number	v1 (current)
This version publication date	03 April 2019
First version publication date	03 April 2019

Trial information

Trial identification

Sponsor protocol code	EXP-1377

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03325296
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	26 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2018
Global end of trial reached?	Yes
Global end of trial date	16 May 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of twice daily topical LEO 124249 ointment 30 mg/g compared with LEO 124249 ointment vehicle on hair growth in subjects with alopecia areata on eyebrows.

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly, 1964, and the amendment from Somerset West, South Africa, October 1996. All subjects received written and verbal information concerning the clinical trial. Subjects were asked to consent that their personal data were recorded, collected, processed and could be transferred to other countries in accordance with any national legislation regulating privacy and data protection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2017
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	Denmark: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	0
Adults (18-64 years)	13
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects were recruited in Denmark, at 2 sites, between 7-Nov-2017 and 22-Mar-2018.

Pre-assignment

Screening details:

Main inclusion criteria: clinical unequivocal diagnosis of alopecia areata (AA), maximal duration of current disease episode of 3 years and no ongoing eyebrow hair growth at study start
Main exclusion criteria: diffuse type AA, subjects with skin condition(s) or use of treatments which could put subject at risk or interfere with trial assessments

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

The packaging and labelling of the 2 investigational medical products contained no evidence of their identity. There is a slight colour difference between the products. However, the difference is only discernible on close inspection with both products compared side by side. Neither the subject nor the investigator were allowed to see the 2 products at the same time. Subjects from the same household were not allowed to participate.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 124249 ointment 30 mg/g

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LEO 124249 ointment 30 mg/g
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Twice daily topical application on both eyebrows for 12 weeks

Arm title	LEO 124249 ointment vehicle

Arm description: -

Arm type	Placebo
Investigational medicinal product name	LEO 124249 ointment vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Twice daily topical application on both eybrows for 12 weeks

Number of subjects in period 1	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle
Started	9	4
Completed	8	3
Not completed	1	1
Trial ended prematurely	1	1

Baseline characteristics

Reporting groups	
Reporting group title	LEO 124249 ointment 30 mg/g
Reporting group description: -	
Reporting group title	LEO 124249 ointment vehicle
Reporting group description: -	

Reporting group values	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle	Total
Number of subjects	9	4	13
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)	0	0	0
Adults (18-64 years)	9	4	13
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	42.8	45.0	
standard deviation	± 12.2	± 11.5	-
Gender categorical Units: Subjects			
Female	4	3	7
Male	5	1	6

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

Subject analysis set description:

The full analysis set includes all randomised subjects. The safety analysis set includes the randomised subjects who received at least 1 application of the investigational medicinal product. This set is identical to the full analysis set.

Reporting group values	Full analysis set		
Number of subjects	13		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	13		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	43.5		
standard deviation	± 11.6		
Gender categorical			
Units: Subjects			
Female	7		
Male	6		

End points

End points reporting groups

Reporting group title	LEO 124249 ointment 30 mg/g
Reporting group description: -	
Reporting group title	LEO 124249 ointment vehicle
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set includes all randomised subjects. The safety analysis set includes the randomised subjects who received at least 1 application of the investigational medicinal product. This set is identical to the full analysis set.

Primary: Change from baseline to Week 12 of investigator evaluated overall area score of eyebrow hair growth

End point title	Change from baseline to Week 12 of investigator evaluated overall area score of eyebrow hair growth[1]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Week 12

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 provided due to lack of efficacy, as demonstrated by an unplanned blinded futility analysis.

End point values	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	4		
Units: area score				
arithmetic mean (standard deviation)	0.0 (± 0.5)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-emergent adverse events

End point title	Treatment-emergent adverse events

End point description:

The treatment-emergent adverse events include adverse events relating to local tolerability.

End point type	Secondary

End point timeframe:

Day 1 to Week 16

End point values	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	4		
Units: number of events	7	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From subject signing inform consent form to Week 16	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1
Reporting groups	
Reporting group title	LEO 124249 ointment 30 mg/g
Reporting group description: -	
Reporting group title	LEO 124249 ointment vehicle
Reporting group description: -	

Serious adverse events	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pilonidal cyst			
subjects affected / exposed	1 / 9 (11.11%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	LEO 124249 ointment 30 mg/g	LEO 124249 ointment vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	2 / 4 (50.00%)	
Injury, poisoning and procedural complications			
Face injury			
subjects affected / exposed	1 / 9 (11.11%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Application site pruritus subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	1 / 4 (25.00%) 1	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 4 (25.00%) 1	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 4 (0.00%) 0	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 4 (25.00%) 1	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 4 (0.00%) 0	
Infections and infestations Influenza subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2 0 / 9 (0.00%) 0	0 / 4 (0.00%) 0 1 / 4 (25.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 February 2018	The main reason for this amendment was to revise 2 of the inclusion criteria to reduce the number of screening failures and to aid recruitment into the trial.
28 March 2018	The main reason for this amendment was to revise 1 of the exclusion criteria to align with the first amendment. The factor 'site' was added to the statistical analysis model. In addition, informed consent date and demographics were added to the data that must be collected for screening failures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 May 2018	An unplanned futility analysis was conducted and on the basis of this analysis the trial was terminated prior to completion. For this reason, the trial was reported as an abbreviated report in accordance with ICH E3. Results for 2 secondary efficacy endpoints were therefore neither analysed nor reported.	-

Notes:

Limitations and caveats

None reported