Clinical trial results:
A phase 2a, randomised, double-blind, placebo-controlled, multi-site, proof of concept trial to evaluate the efficacy and safety of LEO 138559 in adult subjects with moderate to severe atopic dermatitis (AD).

Summary

EudraCT number	2020-005541-16
Trial protocol	DE
Global end of trial date	26 September 2022

Results information

Result version number	v1 (current)
This version publication date	18 June 2023
First version publication date	18 June 2023

Trial information

Trial identification

Sponsor protocol code	LP0145-1376

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, LEO Pharma A/S, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure, LEO Pharma A/S, 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	11 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2022
Global end of trial reached?	Yes
Global end of trial date	26 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of LEO 138559 with placebo in subjects with moderate to severe AD.

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki, the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, in compliance with the approved protocol, and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2021
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: 35
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	58
EEA total number of subjects	44

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)	58
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

58 participants from 19 sites in 4 countries (Canada, Germany, Poland, and the United States of America) were randomized in this trial. The first participant was screened on 14-Jul-2021 and the last participant completed the trial on 26-Sep-2022.

Pre-assignment

Screening details:

76 participants were screened in this trial. Of these, 18 participants (23.7%) were excluded prior to randomization. The main reason for exclusion prior to randomization was eligibility criteria not met (17.1%).

Period 1

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

Blinding implementation details:

This was a double-blinded trial in which LEO 138559 and placebo were visually distinct from each other and not matched for viscosity. IMP was administered by an unblinded trial staff member who was not involved in the trial assessments.

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 138559

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LEO 138559
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

LEO 138559 was given every 2 weeks (Q2W) as 3 SC injections (each 1.0 mL) until Week 14. In addition to the Q2W dosing schedule, an additional dose was given at Week 1.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A dose of 3 SC injections (each 1.0 mL) was given Q2W until Week 14. In addition to the Q2W dosing schedule, an additional dose was given at Week 1.

Number of subjects in period 1	LEO 138559	Placebo
Started	29	29
Completed	22	16
Not completed	7	13
Consent withdrawn by subject	4	10
Adverse event, non-fatal	2	2
Multiple reasons	1	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	LEO 138559
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	LEO 138559	Placebo	Total
Number of subjects	29	29	58
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)	29	29	58
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	38.1	32.8	
standard deviation	± 12.1	± 10.2	-
Gender categorical Units: Subjects			
Female	17	16	33
Male	12	13	25
Baseline disease severity Units: Subjects			
Baseline EASI score <21	14	13	27
Baseline EASI score ≥21	15	16	31
vIGA-AD Units: Subjects			
Moderate	17	20	37
Severe	12	9	21
EASI Units: Score on a scale			
arithmetic mean	26.93	26.12	
standard deviation	± 11.77	± 9.80	-
BSA Units: Percentage			
arithmetic mean	40.2	38.6	
standard deviation	± 21.4	± 18.5	-
Worst daily pruritus NRS (weekly average) Units: Units on a scale			

arithmetic mean	7.57	7.53	
standard deviation	± 1.63	± 1.56	-
POEM			
Units: Units on a scale			
arithmetic mean	22.4	19.2	
standard deviation	± 4.7	± 5.4	-
DLQI			
Units: Units on a scale			
arithmetic mean	17.1	14.0	
standard deviation	± 7.7	± 6.0	-

End points

End points reporting groups

Reporting group title	LEO 138559
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change in EASI Score From Baseline to Week 16

End point title	Change in EASI Score From Baseline to Week 16
End point description:	
The Eczema Area and Severity Index (EASI) is a validated measure used in clinical trials to evaluate the extent and severity of atopic dermatitis. EASI is a composite score ranging from 0 to 72 with higher scores indicating a more extensive and/or severe condition.	
End point type	Primary
End point timeframe:	
Week 0 to Week 16	

End point values	LEO 138559	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: Score on a scale				
arithmetic mean (standard error)	-15.3 (± 2.64)	-3.5 (± 2.91)		

Statistical analyses

Statistical analysis title	LEO 138559 vs Placebo
Comparison groups	Placebo v LEO 138559
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.003 [2]
Method	ANCOVA
Parameter estimate	Median difference (net)
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	-4.1

Notes:

[1] - Two-sided hypotheses were tested based on the pre-specified primary analysis for the primary estimand. The primary estimand used a hypothetical strategy evaluating the treatment difference as if all subjects adhered to the treatment regimen, i.e. they did not discontinue IMP

permanently, did not initiate rescue treatment, or did not have more than one missed treatment dose related to COVID-19.
[2] - The type I error rate of the two-sided hypothesis test was controlled at the 5% significance level.

ANCOVA model: Change in EASI = Treatment + Region + Baseline EASI. Missing values and data 'treated as missing' were imputed using MI assuming MAR.

Secondary: Number of Treatment-emergent Adverse Events From Baseline to Week 16 Per Participant

End point title	Number of Treatment-emergent Adverse Events From Baseline to Week 16 Per Participant

End point description:

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	LEO 138559	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: Number of adverse events	40	26		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 32 weeks (Treatment period: Week 0 to Week 16; Safety follow-up period: Week 16 to Week 32)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	LEO 138559
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	LEO 138559	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	LEO 138559	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 29 (72.41%)	14 / 29 (48.28%)	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Vaccination complication			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Headache			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Syncope			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 29 (3.45%)	2 / 29 (6.90%)	
occurrences (all)	1	3	
Inflammation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Injection site reaction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	1 / 29 (3.45%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Dermatitis acneiform			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Dermatitis atopic			
subjects affected / exposed	4 / 29 (13.79%)	4 / 29 (13.79%)	
occurrences (all)	5	4	
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	2 / 29 (6.90%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	

Renal and urinary disorders			
Renal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	
occurrences (all)	4	0	
Bursitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 29 (20.69%)	2 / 29 (6.90%)	
occurrences (all)	6	2	
Conjunctivitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Coronavirus infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Eczema herpeticum			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Nasopharyngitis			
subjects affected / exposed	3 / 29 (10.34%)	3 / 29 (10.34%)	
occurrences (all)	3	3	
Rhinitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	5 / 29 (17.24%)	
occurrences (all)	1	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2021	The purpose of this protocol amendment was to allow for the clarification and addition of eligibility criteria and the inclusion of additional safety assessments.
31 January 2022	The main purpose for this protocol amendment was to change the event of a positive SARS CoV-2 test (COVID-19) from leading to permanent discontinuation of IMP to leading to a possible temporary discontinuation of IMP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported