Clinical trial results:
Phase 2a trial to assess the efficacy and safety of LEO 152020 in adult patients with cholinergic urticaria

Summary

EudraCT number	2020-004961-38
Trial protocol	DE
Global end of trial date	11 July 2022

Results information

Result version number	v1
This version publication date	27 July 2023
First version publication date	27 July 2023

Trial information

Trial identification

Sponsor protocol code	EXP-2177

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04853992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LEO Pharma A/S
Sponsor organisation address	Industriparken 55, Ballerup, Denmark,
Public contact	Clinical Disclosure, LEO Pharma A/S, +45 4494 5888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure, LEO Pharma A/S, +45 4494 5888, 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	10 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2022
Global end of trial reached?	Yes
Global end of trial date	11 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the efficacy of LEO 152020 compared with placebo in patients with cholinergic urticaria.

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	01 April 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	Germany: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total number of 29 subjects were screened and thereof, 20 subjects in 4 trial sites were randomly assigned stratified by site to one of the two treatment sequences with a ratio of 1:1.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Active

Arm description:

This is a cross over study with two treatment periods. All participants received Active, either in the first or second treatment period and Placebo in the other period.
There were 20 participants that started the trial.
11 were randomised to the sequence Placebo-Active. 1 was withdrawn after completing treatment with Active as they met an exclusion criteria before the start of the second (Placebo) treatment.
9 were randomised to the sequence Active-Placebo. 1 withdrew due to an AE (COVID-19) during the first (Placebo) treatment period.

Arm type	Experimental
Investigational medicinal product name	LEO 152020
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Twice a day for 7 days

Arm title	Placebo

Arm description:

This is a cross over study with two treatment periods. All participants received Placebo, either in the first or second treatment period and Active in the other period.
There were 20 participants that started the trial.
11 were randomised to the sequence Placebo-Active. 1 was withdrawn after completing treatment with Active as they met an exclusion criteria before the start of the second (Placebo) treatment.
9 were randomised to the sequence Active-Placebo. 1 withdrew due to an AE (COVID-19) during the first (Placebo) treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Twice a day for 7 days

Number of subjects in period 1	Active	Placebo
Started	20	20
Completed	18	18
Not completed	2	2
Adverse event, non-fatal	1	1
Met exclusion criteria for second treatment phase	1	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	20	20	
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)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	25		
full range (min-max)	20 to 56	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	14	14	

End points

End points reporting groups

Reporting group title	Active

Reporting group description:

This is a cross over study with two treatment periods. All participants received Active, either in the first or second treatment period and Placebo in the other period.
There were 20 participants that started the trial.
11 were randomised to the sequence Placebo-Active. 1 was withdrawn after completing treatment with Active as they met an exclusion criteria before the start of the second (Placebo) treatment.
9 were randomised to the sequence Active-Placebo. 1 withdrew due to an AE (COVID-19) during the first (Placebo) treatment period.

Reporting group title	Placebo

Reporting group description:

This is a cross over study with two treatment periods. All participants received Placebo, either in the first or second treatment period and Active in the other period.
There were 20 participants that started the trial.
11 were randomised to the sequence Placebo-Active. 1 was withdrawn after completing treatment with Active as they met an exclusion criteria before the start of the second (Placebo) treatment.
9 were randomised to the sequence Active-Placebo. 1 withdrew due to an AE (COVID-19) during the first (Placebo) treatment period.

Primary: Change from baseline in post-provocation Urticaria Activity Score (UASprovo).

End point title	Change from baseline in post-provocation Urticaria Activity Score (UASprovo).

End point description:

End point type	Primary

End point timeframe:

Baseline to day 7

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	18		
Units: UASprovo				
least squares mean (standard deviation)	-1.1 (± 2.1)	-0.5 (± 1.7)		

Statistical analyses

Statistical analysis title	Active vs Placebo
Comparison groups	Active v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.277
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[1] - The primary endpoint, change from baseline in post-provocation Urticaria Activity Score (UASprovo) to the end of the treatment period, was compared between treatments with the null hypothesis that they are equal against the alternative that they are different. The primary efficacy endpoint was analysed using a linear mixed model, containing treatment, period and carryover effects, the factor site and additionally the value of UASprovo at baseline as a covariate.

This is a cross over study.

Secondary: Number of Treatment Emergent Adverse Events

End point title	Number of Treatment Emergent Adverse Events

End point description:

End point type	Secondary

End point timeframe:

From treatment period start to 3 days after treatment end

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: AEs	12	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first trial related activity to the end of trial	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	Active
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (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	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 19 (47.37%)	5 / 19 (26.32%)	
Investigations			
Blood immunoglobulin E increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Low density lipoprotein increased			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 19 (5.26%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 19 (10.53%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 19 (15.79%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 19 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2021	Due to recommendations from BfArM including clarification of standard doses of antihistamines, contraception and pregnancy testing, additional ECG measurements, and benefit/risk assessment.
16 April 2021	To clarify some inconsistencies and the intent of the original protocol e.g. definition of the screening period, visits after early termination, description of CholUAS7.
15 June 2021	Exclusion criterion 18 was changed to allow patients to continue topical use of antihistamines if necessary to treat concomitant allergies.
09 March 2022	Due to a change of location and the new foundation of the Institute of Allergy Research of the Charité (Institute of Allergology IFA).
08 April 2022	With the introduction of COVID-19 vaccines, COVID-19 may now be considered more like other influenza-like diseases – and COVID-19 (confirmed by a positive SARS-CoV-2 test result) is no longer deemed a major health risk as disease symptoms are commonly only mild and patients rapidly recover from COVID-19. This amendment was intended to take account for the changed status of the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported