



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 | v2 |
| This version publication date | 05 April 2024 |
| First version publication date | 27 July 2023 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setCorrection of data |

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: scores on a scale | | | | |
| least squares mean (standard deviation) | -1.1 (± 2.1) | -0.5 (± 1.7) | | |

Statistical analyses

| | |
|----------------------------|-------------------|
| Statistical analysis title | Active vs Placebo |
| Comparison groups | Placebo v Active |

| | |
|---|----------------------------|
| 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 (net) |
| 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 | 9 | 5 | | |

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 | Placebo |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|--------|
| Reporting group title | Active |
|-----------------------|--------|

Reporting group description: -

| Serious adverse events | Placebo | Active | |
|---|----------------|----------------|--|
| 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 | Placebo | Active | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 19 (31.58%) | 9 / 19 (47.37%) | |
| Investigations | | | |
| Blood immunoglobulin E increased | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 19 (5.26%) | |
| occurrences (all) | 0 | 1 | |
| Electrocardiogram ST segment elevation | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 19 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Low density lipoprotein increased | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 19 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |

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

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