# Clinical trial results:
# Interventional, randomized, double-blind, parallel-group, placebo-controlled study of Lu AG09222 for the prevention of migraine in patients with unsuccessful prior preventive treatments

## Summary

| | |
|---|---|
| EudraCT number | 2020-005924-12 |
| Trial protocol | SK CZ DK PL |
| Global end of trial date | 16 March 2023 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 27 March 2024 |
| First version publication date | 27 March 2024 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 19678A |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05133323 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | H. Lundbeck A/S |
| Sponsor organisation address | Ottiliavej 9, Valby, Denmark, 2500 |
| Public contact | Email contact via, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.com |
| Scientific contact | Email contact via, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@Lundbeck.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 | 16 March 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 March 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the trial was to evaluate the efficacy of Lu AG09222 for the prevention of migraine in participants with unsuccessful prior preventive treatments.

Protection of trial subjects:

This study was designed in accordance with the Declaration of Helsinki.

This study was conducted in compliance with the protocol, Good Clinical Practice, and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 11 November 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Czechia: 52 |
| Country: Number of subjects enrolled | Denmark: 11 |
| Country: Number of subjects enrolled | Georgia: 86 |
| Country: Number of subjects enrolled | Poland: 60 |
| Country: Number of subjects enrolled | Slovakia: 23 |
| Country: Number of subjects enrolled | United States: 5 |
| Worldwide total number of subjects | 237 |
| EEA total number of subjects | 146 |

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) | 235 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 237 participants were enrolled in 6 countries.

### 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 |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Lu AG09222 High Dose |

Arm description:

Participants received a single dose of Lu AG09222 by intravenous (IV) infusion.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Lu AG09222 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received a single dose by IV infusion

| | |
|---|---|
| **Arm title** | Lu AG09222 Low Dose |

Arm description:

Participants received a single dose of Lu AG09222 by IV infusion.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Lu AG09222 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received a single dose by IV infusion

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Participants received a single dose of placebo matching to Lu AG09222 by IV infusion.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received a single dose of Lu AG09222-matching placebo (0.9% saline solution) by IV

infusion.

| **Number of subjects in period 1** | Lu AG09222 High Dose | Lu AG09222 Low Dose | Placebo |
|---|---|---|---|
| Started | 97 | 46 | 94 |
| Received at least 1 dose of study drug | 97 | 46 | 94 |
| Completed | 95 | 45 | 93 |
| Not completed | 2 | 1 | 1 |
| Consent withdrawn by subject | 2 | 1 | - |
| Lack of efficacy | - | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Lu AG09222 High Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by intravenous (IV) infusion. | |
| Reporting group title | Lu AG09222 Low Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by IV infusion. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received a single dose of placebo matching to Lu AG09222 by IV infusion. | |

| Reporting group values | Lu AG09222 High Dose | Lu AG09222 Low Dose | Placebo |
|---|---|---|---|
| Number of subjects | 97 | 46 | 94 |
| Age categorical<br>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) | 95 | 46 | 94 |
| From 65-84 years | 2 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 42.5 | 42.5 | 42.5 |
| standard deviation | ± 9.88 | ± 9.35 | ± 9.51 |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 89 | 38 | 81 |
| Male | 8 | 8 | 13 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 97 | 46 | 94 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 237 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>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) | 235 | | |
| From 65-84 years | 2 | | |
| 85 years and over | 0 | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 208 | | |
| Male | 29 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 0 | | |
| White | 237 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 0 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Lu AG09222 High Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by intravenous (IV) infusion. | |
| Reporting group title | Lu AG09222 Low Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by IV infusion. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received a single dose of placebo matching to Lu AG09222 by IV infusion. | |

### Primary: Change From Baseline in the Number of Monthly Migraine Days (MMDs)

| | |
|---|---|
| End point title | Change From Baseline in the Number of Monthly Migraine Days (MMDs) |

End point description:

The Migraine Day definition was based on the International Headache Society (IHS) guidelines for controlled trials of preventive treatment of chronic migraine and episodic migraine in adults. A Migraine Day was defined as a day with a headache that:

- lasts ≥4 hours and meets International Classification of Headache Disorders Third Edition (ICHD-3) guidelines criteria C and D for migraine without aura
- or lasts ≥30 minutes and where the participant had an aura with the headache (migraine with aura),
- or lasts ≥30 minutes and meets two of the three ICHD-3 criteria B (without the condition on 72 hours), C and D for migraine without aura (probable migraine),
- or a day with a headache that is successfully treated with a triptan, ergotamine, or other migraine-specific acute medication.

The all participants treated set (APTS) represents all randomized participants who received an infusion of investigational medicinal product.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Baseline, Week 4

| End point values | Lu AG09222 High Dose | Lu AG09222 Low Dose | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 97 | 46 | 94 | |
| Units: days | | | | |
| least squares mean (standard error) | -6.2 (± 0.66) | -6.0 (± 0.94) | -4.2 (± 0.67) | |

### Statistical analyses

| Statistical analysis title | Change from Baseline in Monthly Migraine Days |
|---|---|
| Comparison groups | Lu AG09222 High Dose v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0106 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | 90 % |
| sides | 1-sided |
| upper limit | -0.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.89 |

## Secondary: Change From Baseline in the Number of Monthly Headache Days (MHDs)

| | |
|---|---|
| End point title | Change From Baseline in the Number of Monthly Headache Days (MHDs) |

End point description:

A Headache Day was defined as a day with a headache that lasted ≥30 minutes or that meets the definition of a Migraine Day.
The APTS represents all randomized participants who received an infusion of investigational medicinal product.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Week 4

| End point values | Lu AG09222 High Dose | Lu AG09222 Low Dose | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 96 | 44 | 93 | |
| Units: days | | | | |
| least squares mean (standard error) | -5.8 (± 0.65) | -5.9 (± 0.93) | -4.1 (± 0.67) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With ≥50% Reduction From Baseline in MMDs

| | |
|---|---|
| End point title | Percentage of Participants With ≥50% Reduction From Baseline in MMDs |

End point description:

The Migraine Day definition was based on the International Headache Society (IHS) guidelines for controlled trials of preventive treatment of chronic migraine and episodic migraine in adults. A Migraine Day was defined as a day with a headache that:

- lasts ≥4 hours and meets International Classification of Headache Disorders Third Edition (ICHD-3) guidelines criteria C and D for migraine without aura

• or lasts ≥30 minutes and where the participant had an aura with the headache (migraine with aura),
• or lasts ≥30 minutes and meets two of the three ICHD-3 criteria B (without the condition on 72 hours), C and D for migraine without aura (probable migraine),
• or a day with a headache that is successfully treated with a triptan, ergotamine, or other migraine-specific acute medication.
The APTS represents all randomized participants who received an infusion of investigational medicinal product.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 4

| **End point values** | Lu AG09222 High Dose | Lu AG09222 Low Dose | Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 97 | 46 | 94 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 32.2 | 36.1 | 26.8 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Up to 12 weeks | |
| Adverse event reporting additional description: | |
| The APTS represents all randomized participants who received an infusion of investigational medicinal product. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Lu AG09222 High Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by intravenous (IV) infusion. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received a single dose of placebo matching to Lu AG09222 by IV infusion. | |
| Reporting group title | Lu AG09222 Low Dose |
| Reporting group description: | |
| Participants received a single dose of Lu AG09222 by IV infusion. | |

| Serious adverse events | Lu AG09222 High Dose | Placebo | Lu AG09222 Low Dose |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | 0 / 94 (0.00%) | 0 / 46 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Musculoskeletal and connective tissue disorders | | | |
| Sympathetic Posterior Cervical Syndrome | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | 0 / 94 (0.00%) | 0 / 46 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Lu AG09222 High Dose | Placebo | Lu AG09222 Low Dose |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 97 (18.56%) | 8 / 94 (8.51%) | 4 / 46 (8.70%) |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | 1 / 94 (1.06%) | 2 / 46 (4.35%) |
| occurrences (all) | 5 | 1 | 2 |
| Infections and infestations | | | |
| Covid-19 | | | |
| subjects affected / exposed | 7 / 97 (7.22%) | 3 / 94 (3.19%) | 2 / 46 (4.35%) |
| occurrences (all) | 7 | 3 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 7 / 97 (7.22%) | 4 / 94 (4.26%) | 0 / 46 (0.00%) |
| occurrences (all) | 7 | 5 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 24 January 2022 | Updated exploratory objectives and clarified inclusion/exclusion criteria. |
| 11 July 2022 | Deleted all descriptions of and references to the non-binding interim analysis for futility, as decision was taken not to conduct an interim analysis. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported