



## 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
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#### 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
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<b>Arm title</b>	Lu AG09222 High Dose
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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

<b>Arm title</b>	Lu AG09222 Low Dose
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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

<b>Arm title</b>	Placebo
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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.

<b>Number of subjects in period 1</b>	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			
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			
Units: years			
arithmetic mean	42.5	42.5	42.5
standard deviation	± 9.88	± 9.35	± 9.51
Sex: Female, Male			
Units: participants			
Female	89	38	81
Male	8	8	13
Race (NIH/OMB)			
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 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 Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: participants			
Female	208		
Male	29		
Race (NIH/OMB) 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:	
<ul style="list-style-type: none"><li>• lasts <math>\geq 4</math> hours and meets International Classification of Headache Disorders Third Edition (ICHD-3) guidelines criteria C and D for migraine without aura</li><li>• or lasts <math>\geq 30</math> minutes and where the participant had an aura with the headache (migraine with aura),</li><li>• or lasts <math>\geq 30</math> 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),</li><li>• or a day with a headache that is successfully treated with a triptan, ergotamine, or other migraine-specific acute medication.</li></ul>	
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 ( $\pm$ 0.66)	-6.0 ( $\pm$ 0.94)	-4.2 ( $\pm$ 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 $\geq 30$ 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 ( $\pm$ 0.65)	-5.9 ( $\pm$ 0.93)	-4.1 ( $\pm$ 0.67)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With $\geq 50\%$ Reduction From Baseline in MMDs

End point title	Percentage of Participants With $\geq 50\%$ 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: <ul style="list-style-type: none"> <li>lasts <math>\geq 4</math> hours and meets International Classification of Headache Disorders Third Edition (ICHD-3) guidelines criteria C and D for migraine without aura</li> </ul>	

- or lasts  $\geq 30$  minutes and where the participant had an aura with the headache (migraine with aura),
- or lasts  $\geq 30$  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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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### Reporting groups

Reporting group title	Lu AG09222 High Dose
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Reporting group description:

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

Reporting group title	Placebo
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Reporting group description:

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

Reporting group title	Lu AG09222 Low Dose
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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:

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**Interruptions (globally)**

Were there any global interruptions to the trial? No

**Limitations and caveats**

None reported