



## Clinical trial results:

### The effect of anti-calcitonin gene-related peptide (CGRP) receptor antibodies on the headache inducing properties of CGRP and cilostazol in migraine patients

#### Summary

EudraCT number	2020-000661-16
Trial protocol	DK
Global end of trial date	17 January 2022

#### Results information

Result version number	v1 (current)
This version publication date	16 May 2023
First version publication date	16 May 2023

#### Trial information

##### Trial identification

Sponsor protocol code	CGRP2020
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04452929
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Rigshospitalet Glostrup
Sponsor organisation address	Valdemar Hansens Vej 5, Glostrup, Denmark,
Public contact	Thien Phu Do, Rigshospitalet Glostrup, thiendo@gmail.com
Scientific contact	Thien Phu Do, Rigshospitalet Glostrup, thiendo@gmail.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	Interim
Date of interim/final analysis	04 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2022
Global end of trial reached?	Yes
Global end of trial date	17 January 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

- (1) To investigate the effect of anti-CGRP receptor monoclonal antibody (mAb), erenumab, in prevention of CGRP-induced and cilostazol-induced migraine-like attacks in patients with migraine
- (2) To investigate the effect of anti-CGRP receptor mAb, erenumab, in prevention of CGRP-induced and cilostazol-induced dilation of extracerebral arteries in patients with migraine
- (3) To investigate the effect of anti-CGRP receptor mAb, erenumab, in preventing CGRP-induced and cilostazol-induced facial flushing in patients with migraine
- (4) To investigate the effect of anti-CGRP receptor mAb, erenumab, on peptide blood levels in patients with migraine

Protection of trial subjects:

The protocol was approved by the Regional Health Research Ethics Committee of the Capital Region of Denmark (identifier: H-19073983), the Danish Data Protection Agency (P-2020-652), and the Danish Medicines Agency (identifier: 2020033418). We obtained a signed consent form at the time of screening before any protocol-related procedures or assessments. All study-related procedures complied with the Declaration of Helsinki, with later revisions. The study is registered in ClinicalTrials.gov (identifier: NCT04452929).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2020
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	Denmark: 75
Worldwide total number of subjects	75
EEA total number of subjects	75

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)	75
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	75
Number of subjects completed	75

### Period 1

Period 1 title	Erenumab or placebo
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

We enrolled participants in a randomized, double-blind, placebo-controlled, parallel trial at a single center in Denmark. Participants were randomly allocated to a subcutaneous administration of 140mg of erenumab or placebo (isotonic saline). Erenumab was provided by Novartis Pharma AG (Basel, Switzerland) and sorted in blinded packaging by Nomeco A/S (Copenhagen, Denmark). Independent pharmacy staff were responsible for randomization and allocation concealment.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Erenumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	erenumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

140mg

<b>Arm title</b>	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Isotonic saline

Number of subjects in period 1	Erenumab	Placebo
Started	37	38
Completed	37	38

## Period 2

Period 2 title	CGRP
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor, Carer, Monitor

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Erenumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	calcitonin gene-related peptide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5µg/min of CGRP over 20 minutes

<b>Arm title</b>	Placebo
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Arm description: -

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

Dosage and administration details:

1.5µg/min of CGRP over 20 minutes

Number of subjects in period 2	Erenumab	Placebo
Started	37	38
Completed	37	38

<b>Period 3</b>	
Period 3 title	Cilostazol
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor, Carer, Monitor
<b>Arms</b>	
Are arms mutually exclusive?	Yes
<b>Arm title</b>	Erenumab
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cilostazol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 200mg	
<b>Arm title</b>	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	cilostazol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 200mg	

Number of subjects in period 3	Erenumab	Placebo
Started	37	38
Completed	37	38

## Baseline characteristics

### Reporting groups

Reporting group title	Erenumab or placebo
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Reporting group description: -

Reporting group values	Erenumab or placebo	Total	
Number of subjects	75	75	
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)	75	75	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	33.4		
standard deviation	± 11.1	-	
Gender categorical			
Units: Subjects			
Female	66	66	
Male	9	9	

## End points

### End points reporting groups

Reporting group title	Erenumab
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Erenumab
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Erenumab
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

### Primary: Migraine attack following cilostazol

End point title	Migraine attack following cilostazol
End point description:	
End point type	Primary
End point timeframe:	
Incidence of migraine attacks in a 12-hour observational period after administration of experimental triggers	

End point values	Erenumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	38		
Units: Migraine attack	28	31		

### Statistical analyses

Statistical analysis title	Migraine attack induction rate
Comparison groups	Placebo v Erenumab
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.024
Method	Chi-squared



**Primary: Migraine attack following calcitonin gene-related peptide**

End point title	Migraine attack following calcitonin gene-related peptide
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End point description:

End point type	Primary
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End point timeframe:

Incidence of migraine attacks in a 12-hour observational period after administration of experimental triggers

End point values	Erenumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	38		
Units: Migraine attack	28	31		

**Statistical analyses**

<b>Statistical analysis title</b>	Migraine attack induction rate
Comparison groups	Erenumab v Placebo
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.24
Method	Chi-squared

**Secondary: Headache following cilostazol**

End point title	Headache following cilostazol
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End point description:

End point type	Secondary
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End point timeframe:

Incidence of headache in a 12-hour observational period after administration of experimental triggers

End point values	Erenumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	38		
Units: Headache	33	37		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Headache following calcitonin gene-related peptide

End point title	Headache following calcitonin gene-related peptide
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End point description:

End point type	Secondary
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End point timeframe:

Incidence of headache in a 12-hour observational period after administration of experimental triggers

End point values	Erenumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	38		
Units: Headache	24	35		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Incidence of adverse events in a 12-hour observational period after administration of experimental triggers

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

### Reporting groups

Reporting group title	Erenumab - Cilostazol
Reporting group description: -	
Reporting group title	Erenumab - Calcitonin gene-related peptide
Reporting group description: -	
Reporting group title	Placebo - Cilostazol
Reporting group description: -	
Reporting group title	Placebo - Calcitonin gene-related peptide
Reporting group description: -	

Serious adverse events	Erenumab - Cilostazol	Erenumab - Calcitonin gene-related peptide	Placebo - Cilostazol
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo - Calcitonin gene-related peptide		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Erenumab - Cilostazol	Erenumab - Calcitonin gene-related peptide	Placebo - Cilostazol
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)	15 / 37 (40.54%)	13 / 38 (34.21%)

Cardiac disorders			
Palpitations			
subjects affected / exposed	9 / 37 (24.32%)	6 / 37 (16.22%)	6 / 38 (15.79%)
occurrences (all)	9	6	6
General disorders and administration site conditions			
Cold sensations			
subjects affected / exposed	1 / 37 (2.70%)	0 / 37 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Warm sensations			
subjects affected / exposed	15 / 37 (40.54%)	15 / 37 (40.54%)	13 / 38 (34.21%)
occurrences (all)	15	15	13
Ear and labyrinth disorders			
Dizziness			
subjects affected / exposed	2 / 37 (5.41%)	1 / 37 (2.70%)	2 / 38 (5.26%)
occurrences (all)	2	1	2
Ear fullness			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eyes			
subjects affected / exposed	0 / 37 (0.00%)	1 / 37 (2.70%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 37 (2.70%)	0 / 37 (0.00%)	1 / 38 (2.63%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Flushing			
subjects affected / exposed	0 / 37 (0.00%)	4 / 37 (10.81%)	0 / 38 (0.00%)
occurrences (all)	0	4	0
Itch			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Placebo - Calcitonin gene-related peptide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 38 (97.37%)		

Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	31 / 38 (81.58%) 31		
General disorders and administration site conditions Cold sensations subjects affected / exposed occurrences (all)  Warm sensations subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0  37 / 38 (97.37%) 37		
Ear and labyrinth disorders Dizziness subjects affected / exposed occurrences (all)  Ear fullness subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1  2 / 38 (5.26%) 2		
Eye disorders Dry eyes subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 4		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Skin and subcutaneous tissue disorders Flushing subjects affected / exposed occurrences (all)  Itch subjects affected / exposed occurrences (all)	34 / 38 (89.47%) 34  1 / 38 (2.63%) 1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported