



Clinical trial results: Cabergoline as a Preventive Treatment for Chronic Migraine: an Investigator-Initiated, Randomized Clinical Trial Summary

EudraCT number	2021-005579-38
Trial protocol	DK
Global end of trial date	13 June 2023

Results information

Result version number	v1 (current)
This version publication date	27 June 2024
First version publication date	27 June 2024

Trial information

Trial identification

Sponsor protocol code	1
-----------------------	---

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05525611
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 165, Aarhus N, Denmark, 8200
Public contact	Jens Otto Lunde Jørgensen, Department of Endocrinology, +45 20727383, joj@clin.au.dk
Scientific contact	Jens Otto Lunde Jørgensen, Department of Endocrinology, +45 20727383, joj@clin.au.dk

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	29 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2023
Global end of trial reached?	Yes
Global end of trial date	13 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the effect of Cabergoline in patients with migraine

Protection of trial subjects:

The study was monitored by the Good Clinical Practice Unit at Aarhus University Hospital. All participant were ask about adverse events, and could contact the investigator at any time, if adverse events were experienced.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2022
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: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	36
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled on September 13, 2022, and the last patient completed the study on June 13, 2023. Patients were recruited from the Department of Neurology at Aarhus University Hospital and through the Aarhus University Hospital facebook page.

Pre-assignment

Screening details:

101 adults were screened for eligibility. Forty-five patients failed to meet inclusion criteria (because of too few migraine days, comorbidities, breastfeeding, use of a dopamine antagonist, not using contraception, planned medication changes) and 11 declined to participate.

Period 1

Period 1 title	Baseline period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cabergoline

Arm description: -

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

Dosage and administration details:

0.5 mg once weekly orally

Arm title	Placebo
------------------	---------

Arm description: -

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:

One tablet once a week orally

Number of subjects in period 1	Cabergoline	Placebo
Started	18	18
Completed	18	18

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cabergoline

Arm description:

Cabergoline 0.5 mg once weekly as add-on treatment

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

Dosage and administration details:

0.5 mg once weekly orally

Arm title	Placebo
------------------	---------

Arm description:

Placebo once weekly as add-on treatment

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:

One tablet once a week orally

Number of subjects in period 2	Cabergoline	Placebo
Started	18	18
Completed	18	18

Baseline characteristics

Reporting groups

Reporting group title	Cabergoline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Cabergoline	Placebo	Total
Number of subjects	18	18	36
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)	18	18	36
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41	44	
standard deviation	± 10	± 8	-
Gender categorical Units: Subjects			
Female	17	16	33
Male	1	2	3
Acute headache medication use Units: Subjects			
Acute headache medication use	18	18	36
Migraine-preventive medication use Units: Subjects			
No current or previous use	6	7	13
Previous use only	5	5	10
Current use	7	6	13
History of preventive treatment failure Units: Subjects			
Lack of efficacy or unacceptable side effects	10	9	19
No History of preventive treatment failure	7	7	14
Not recorded	1	2	3
Age at migraine onset Units: year			
arithmetic mean	17.1	17.2	
standard deviation	± 8.7	± 6.0	-

Monthly migraine days Units: day arithmetic mean standard deviation	13.6 ± 4.1	14.0 ± 5.3	-
Days of use of acute migraine medication Units: day arithmetic mean standard deviation	10.5 ± 4.5	11.5 ± 3.1	-
HIT-6 score Units: score arithmetic mean standard deviation	64 ± 5.6	63.8 ± 3.4	-
MIDAS grade Units: Score median inter-quartile range (Q1-Q3)	47 27.5 to 85	43 27 to 58.5	-

End points

End points reporting groups

Reporting group title	Cabergoline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Cabergoline
Reporting group description:	
Cabergoline 0.5 mg once weekly as add-on treatment	
Reporting group title	Placebo
Reporting group description:	
Placebo once weekly as add-on treatment	

Primary: Change in monthly migraine days

End point title	Change in monthly migraine days
End point description:	
End point type	Primary
End point timeframe:	
Change in monthly migraine days from baseline to the last month of the treatment phase	

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: day				
median (inter-quartile range (Q1-Q3))	-5 (-9 to -3)	-3.7 (-5.5 to -1.5)		

Statistical analyses

Statistical analysis title	Mann Whitney U test/unpaired t-test
Statistical analysis description:	
Primary and secondary outcomes were analysed using a linear regression model with heteroscedasticity-robust standard errors, computed via the HC1 method, or unpaired t-test and presented as mean \pm SE, if data were normally distributed. Non-normally distributed data were analysed using Mann Whitney U test and presented as medians (IQR).	
Comparison groups	Cabergoline v Placebo

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Secondary: $\geq 50\%$ Reduction from baseline in monthly migraine days

End point title	$\geq 50\%$ Reduction from baseline in monthly migraine days
End point description:	
End point type	Secondary
End point timeframe:	
From baseline to last month of treatment phase	

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: number	8	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC)

End point title	Patient Global Impression of Change (PGIC)
End point description:	
End point type	Secondary
End point timeframe:	
Last visit (after completion of treatment period)	

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: likert scale				
median (inter-quartile range (Q1-Q3))	8 (6 to 9)	5 (5 to 6.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in acute migraine-specific medication from baseline

End point title	Change in acute migraine-specific medication from baseline
-----------------	------------------------------------------------------------

End point description:

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

End point timeframe:

Change from baseline to last month of treatment phase

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: number				
median (inter-quartile range (Q1-Q3))	-3 (-7 to 0)	-2.5 (-4.5 to -0.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HIT-6 score from baseline

End point title	Change in HIT-6 score from baseline
-----------------	-------------------------------------

End point description:

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

End point timeframe:

Change from baseline to end of treatment phase

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: score				
median (inter-quartile range (Q1-Q3))	-3.8 (-7.5 to 1)	-2.6 (-4 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in MIDAS score from baseline

End point title	Change in MIDAS score from baseline
End point description:	
End point type	Secondary
End point timeframe:	
Change from baseline to end of treatment phase	

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: score				
median (inter-quartile range (Q1-Q3))	-9 (-27.5 to -2.75)	-10 (-32.5 to -2.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in serum prolactin

End point title	Change in serum prolactin
End point description:	
End point type	Secondary
End point timeframe:	
Change from baseline to end of treatment phase	

End point values	Cabergoline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16		
Units: IU/l				
median (inter-quartile range (Q1-Q3))	-112 (-183 to -95)	-0.5 (-44.8 to 37.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded for each patient from inclusion in the trial until four weeks following completion.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	ICD
Dictionary version	10

Reporting groups

Reporting group title	Cabergoline
-----------------------	-------------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Serious adverse events	Cabergoline	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Cabergoline	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)	4 / 18 (22.22%)	
Cardiac disorders			
Chest pain	Additional description: Stabbing chest pain		
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 18 (22.22%)	3 / 18 (16.67%)	
occurrences (all)	4	3	
Dizziness			
subjects affected / exposed	2 / 18 (11.11%)	0 / 18 (0.00%)	
occurrences (all)	2	0	

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 18 (22.22%)	0 / 18 (0.00%)	
occurrences (all)	4	0	
sweating			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Weight gain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 18 (11.11%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Loss of appetite			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported