Clinical trial results:
“Follow the sutures“.
An open multicenter, multinational pilot study to explore tolerability, safety and effect of a new procedure for injecting botulinum toxin in the head against chronic migraine.

Summary

EudraCT number	2017-002516-13
Trial protocol	NO
Global end of trial date	31 December 2020

Results information

Result version number	v1 (current)
This version publication date	19 November 2021
First version publication date	19 November 2021

Trial information

Trial identification

Sponsor protocol code	FollowTheSutures

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03543254
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	St. Olavs Hospital HF
Sponsor organisation address	Olav kyrres gate, TRONDHEIM, Norway, 7006
Public contact	Gøril Bruvik Gravdahl, Nasjonal kompetansetjeneste for hodepine, St. Olavs hospital, 47 72575147, knut.hagen@ntnu.no
Scientific contact	Gøril Bruvik Gravdahl, Nasjonal kompetansetjeneste for hodepine, St. Olavs hospital, 95401579 72575147, knut.hagen@ntnu.no

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 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2020
Global end of trial reached?	Yes
Global end of trial date	31 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether the new injection procedure is safe and tolerable to the patients

Protection of trial subjects:

Drug liability insurance payment for all trials subjects

Background therapy:

Botulinum toxin injection given in a open-label, non-controlled single-center study

Evidence for comparator:

non-controlled design

Actual start date of recruitment	15 May 2018
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	Norway: 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:

Potential study patients were identified among regular outpatients at the Department of Neurology, St. Olavs Hospital in Trondheim, Norway. Planned recruitment of patients at the Mayo Clinic in USA cancelled due to the Covid 19 pandemic

Pre-assignment

Screening details:

Potential participants had been sent an email with the informed consent form which was signed at the screening visit

Period 1

Period 1 title	Baseline period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The study was open-labelled

Arms

Arm title	Baseline period of at least 28 days

Arm description:

Headache diary

Arm type	Headache diary
Investigational medicinal product name	Headache diary
Investigational medicinal product code	
Other name	Headache diary
Pharmaceutical forms	Wound stick
Routes of administration	Topical

Dosage and administration details:

Every days

Number of subjects in period 1	Baseline period of at least 28 days
Started	20
Completed	20

Period 2

Period 2 title	12 weeks follow-up
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-labelled

Arms

Arm title	Botulinum toxin-A

Arm description:

The participants (all women) with a negative pregnancy test got injection of 90 units of botulinum toxin A

Arm type	Active comparator
Investigational medicinal product name	botulinum toxin A
Investigational medicinal product code	
Other name	botulinum toxin A
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Solution for injection

Dosage and administration details:

90 Unit

Number of subjects in period 2	Botulinum toxin-A
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title	Baseline period

Reporting group description:
age and gender

Reporting group values	Baseline period	Total	
Number of subjects	20	20	
Age categorical			
The mean age was40 years (SD) 9, range 19-58			
Units: Subjects			
Adults (18-64 years)	20	20	
Age continuous			
Units: years			
geometric mean	40		
standard deviation	± 9	-	
Gender categorical			
20 women, 0 men			
Units: Subjects			
Female	20	20	
Male	0	0	

Subject analysis sets

Subject analysis set title	Active tratment
Subject analysis set type	Per protocol

Subject analysis set description:
Moderate to severe headache days

Reporting group values	Active tratment		
Number of subjects	20		
Age categorical			
The mean age was40 years (SD) 9, range 19-58			
Units: Subjects			
Adults (18-64 years)	20		
Age continuous			
Units: years			
geometric mean	40		
standard deviation	± 9		
Gender categorical			
20 women, 0 men			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Baseline period of at least 28 days
Reporting group description: Headache diary	
Reporting group title	Botulinum toxin-A
Reporting group description: The participants (all women) with a negative pregnancy test got injection of 90 units of botulinum toxin A	
Subject analysis set title	Active tratment
Subject analysis set type	Per protocol
Subject analysis set description: Moderate to severe headache days	

Primary: Moderate to severe headache at week 5-8 after injection compared to baseline

End point title	Moderate to severe headache at week 5-8 after injection compared to baseline
End point description: Diary information	
End point type	Primary
End point timeframe: Week 5-8 versus baseline	

End point values	Botulinum toxin-A	Active tratment		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19	20		
Units: Headache days				
arithmetic mean (standard deviation)				
Active	11.7 (± 63.8)	11.7 (± 63.8)		

Statistical analyses

Statistical analysis title	Pared t-test
Statistical analysis description: Paired t test and p <0.05 considered statistic significant	
Comparison groups	Botulinum toxin-A v Active tratment
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	5

Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	95
Variability estimate	Standard deviation
Dispersion value	0.05

Notes:

[1] - paired t test

Secondary: Days with headache lasting at least 4 hours

End point title	Days with headache lasting at least 4 hours
End point description:	
Days with headache lasting at lest 4 hours per days	
End point type	Secondary
End point timeframe:	
5-8 weeks versus baseline	

End point values	Botulinum toxin-A	Active tratment		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19	19		
Units: Headache days				
arithmetic mean (standard deviation)	13.8 (± 28.4)	13.8 (± 28.4)		

Statistical analyses

Statistical analysis title	Pared t-test
Comparison groups	Botulinum toxin-A v Active tratment
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	95
Variability estimate	Standard deviation
Dispersion value	0.01

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
12 weeks follow-up	
Adverse event reporting additional description:	
AE during baseline and the first 3 moths after injection	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	1

Reporting groups	
Reporting group title	12 weeks follow up

Reporting group description:

One had reduced power of chewing and several short-lasting neck pain during injection

Serious adverse events	12 weeks follow up		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	12 weeks follow up		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Noe AE reach 5%

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The pilot study should include 40 participants, but only 20 were included due to the Covid 19 pandemic

Notes: