



Clinical trial results:

A phase IV single-blind placebo-controlled cross-over study to investigate the efficacy of greater occipital nerve block with local anaesthetic and steroid in patients with chronic migraine.

Summary

EudraCT number	2014-001115-39
Trial protocol	GB
Global end of trial date	23 January 2020

Results information

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

Trial information

Trial identification

Sponsor protocol code	GON2014/05
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	Trust headquarters Executive Offices Ground Floor Pathology and Pharmacy Building, London, United Kingdom, E1 2ES
Public contact	Dr Vivek Mehta, Barts Health NHS Trust , +44 02034656010, vivek.mehta@nhs.net
Scientific contact	Dr Vivek Mehta , Barts Health NHS Trust, +44 02034656010, vivek.mehta@nhs.net

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	23 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 January 2020
Global end of trial reached?	Yes
Global end of trial date	23 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objective- to investigate any improvement in disability associated with chronic migraine disorder in the two treatment arms (GON block versus placebo procedure.)

Secondary Objective-

- To assess change in participant headache frequency& severity,
- To assess the change in participant anxiety and depression levels,
- To assess the safety and tolerability in the two treatment arms (GON block versus placebo procedure)
- To assess the eligibility criteria recruitment and retention of participants in the two treatment arms.
- To assess the feasibility and acceptability of two treatment arms from the point of view of participants and their pain teams.

Protection of trial subjects:

This study intends to provide more detailed information on the effectiveness, safety and tolerability of GON block with local anaesthetic and steroid in patients with chronic migraine. It does this by comparing it to a dummy(placebo) procedure (a needle is inserted near the nerve, but no therapeutic substance is injected). It is a cross-over study : all patients will receive both the GON block and the dummy procedure(not necessarily in that order), with entail an injection of 2ml of 2% lidocaine (a local anaesthetic) and 80mg of DepoMedrone (a steroid) through a fine needle (a total of 4 mls). The dummy procedure will consist of an injection of 4 mls of normal saline (a solution of common salt and water) through a fine needle

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2018
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	United Kingdom: 8
Worldwide total number of subjects	8
EEA total number of subjects	0

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)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment date: 12/Jul/2018, Patients aged over the age of 18 who are able to provide written consent. Ability to read and write English. Diagnosis of chronic migraine with or without acute relief medication overuse as confirmed by diary documentation.

Pre-assignment

Screening details:

A total 210 patients attended the neurology clinic at site where their suitability for the receive either the GON block (active group) or the placebo injection(control group) using sequentially numbered, opaque, sealed envelopes containing a previously- generated allocation sequence. Only the patients will be blinded to it.

Period 1

Period 1 title	Intervention 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Active treatment (GON Block)

Arm type	Active comparator
Investigational medicinal product name	Depo-Medrone 40mg/mL and Lidocaine Hydrochloride 2% 5mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

4 ml mixture consisting 2 ml of 2% lidocaine and 80ml methylprednisolone

Arm title	Arm B
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Arm description:

Placebo procedure

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride 0.9% w/v 10mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

Sodium Chloride 0.9% w/v 10mL

Number of subjects in period 1	Arm A	Arm B
Started	4	4
Completed	2	1
Not completed	2	3
Consent withdrawn by subject	-	2
unblinded	-	1
Lost to follow-up	2	-

Period 2

Period 2 title	Intervention 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Placebo procedure

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride 0.9% w/v 10mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

Sodium Chloride 0.9% w/v 10mL

Arm title	Arm B
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Arm description:

Active treatment (GON Block)

Arm type	Active comparator
Investigational medicinal product name	Depo-Medrone 40mg/mL and Lidocaine Hydrochloride 2% 5mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

4 ml mixture consisting 2 ml of 2% lidocaine and 80ml methylprednisolone

Number of subjects in period 2	Arm A	Arm B
Started	1	2
Completed	1	2

Baseline characteristics

Reporting groups

Reporting group title	Intervention 1
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Reporting group description: -

Reporting group values	Intervention 1	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	8	8	

Subject analysis sets

Subject analysis set title	McNemar test
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Subject analysis set type	Per protocol
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Subject analysis set description:

McNemar test will be used to assess the treatment differences in categorical variables and paired t test will be employed to evaluate the difference in secondary endpoints between GON and placebo as appropriate. For comparison of non-parametric variables between the GON and placebo, Wilcoxon sign ranked test will be used. Generalized linear mixed model which allow assessment of period and carryover effects from one treatment phase to another will also be applied to evaluate treatment differences in repeated measurements of primary and secondary endpoints. A p value less than 0.05 will be considered statistically significant. All data will be analysed on the intention-to-treat basis and missing values are replaced by the last observed value of that variable.

Reporting group values	McNemar test		
Number of subjects	1		
Age categorical			
Units: Subjects			
Adults (18-64 years)	1		
From 65-84 years	0		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	1		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Active treatment (GON Block)	
Reporting group title	Arm B
Reporting group description:	
Placebo procedure	
Reporting group title	Arm A
Reporting group description:	
Placebo procedure	
Reporting group title	Arm B
Reporting group description:	
Active treatment (GON Block)	
Subject analysis set title	McNemar test
Subject analysis set type	Per protocol
Subject analysis set description:	
McNemar test will be used to assess the treatment differences in categorical variables and paired t test will be employed to evaluate the difference in secondary endpoints between GON and placebo as appropriate. For comparison of non-parametric variables between the GON and placebo, Wilcoxon sign ranked test will be used. Generalized linear mixed model which allow assessment of period and carryover effects from one treatment phase to another will also be applied to evaluate treatment differences in repeated measurements of primary and secondary endpoints. A p value less than 0.05 will be considered statistically significant. All data will be analysed on the intention-to-treat basis and missing values are replaced by the last observed value of that variable.	

Primary: Primary Endpoint

End point title	Primary Endpoint ^[1]
End point description:	
Primary Objective: Improvement in disability associated with chronic migraine disorder.	
Primary End Point:	
- change in Headache Impact Test (HIT-6) score - change in Migraine specific Questionnaire Score (MSQ) - change in the 12-item Short-Form Health Survey (SF-12) Questionnaire	
End point type	Primary
End point timeframe:	
Maximum 24 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: We were unable to reach our object of recruiting 30 randomise patients to the study. Instead, we were only able to recruit 8 patients and had only 3 patients who completed the study. Due to the small number of patients recruited in this feasibility study, there will be no analysis.

End point values	Arm A	Arm B	Arm A	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	1	2
Units: score				
number (not applicable)	2	1	1	2

End point values	McNemar test			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: score				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Endpoints

End point title	Secondary Endpoints
End point description:	
Secondary Objectives:	
- change in Headache frequency& Severity - change in anxiety and depression levels - safety and tolerability - eligibility criteria, recruitment and retention levels - feasibility and acceptability of the two treatment arms	
Secondary Endpoints:	
- Frequency and severity as scored in the HIT-6 questionnaire - Change in Hospital Anxiety and Depression Depression Scores (HADS) - Adverse events - Feedback from clinicians involved in recruitment - Number of participants that complete the study - Questionnaire upon completion of study asking participant if they found the treatment acceptable - Feedback from clinicians regarding overall feasibility and acceptability of two treatment arms	
End point type	Secondary
End point timeframe:	
Maximum 24 weeks	

End point values	Arm A	Arm B	Arm A	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	1	2
Units: score				
number (not applicable)	2	1	1	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Report Adverse Events (AEs) include events starting on or visit 1 until visit 5.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Intervention 2
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Reporting group description: -

Serious adverse events	Intervention 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.13 %

Non-serious adverse events	Intervention 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Infections and infestations			
Headache	Additional description: Patient-reported increased left-sided heading and swelling following an intervention. The patient went to A&E for advice where was admitted for further test. The patient was discharged. Symptoms resolved after a week.		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2017	The changes made in the protocol are mainly to indicate that the MHRA approved labels will no longer be used and that the IMPs involved in the study will be obtained from hospital stock.
28 June 2017	Study extension to 31 July 2018
03 April 2018	Clarification of recruitment sites in the protocol. Added Barts Health NHS Trust as a site.
01 June 2018	Study Extension to Dec 2019

Notes:

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 GON block injections may have a therapeutic effect in controlling migraines. Due to small numbers in study and failure to achieve our expected recruitment target, it is difficult to conclude the hypothesis. Therefore, the study terminated early.

Notes: