Clinical trial results:
The effect of remote ischaemic preconditioning and glyceryl trinitrate on peri-operative myocardial injury in cardiac bypass surgery patients (ERIC-GTN study)- a four arm randomised controlled trial

Summary

EudraCT number	2013-001922-24
Trial protocol	GB
Global end of trial date	03 June 2019

Results information

Result version number	v1 (current)
This version publication date	12 November 2020
First version publication date	12 November 2020

Trial information

Trial identification

Sponsor protocol code	120541

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01864252
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	ower St, Bloomsbury, London, United Kingdom, WC1E 6BT
Public contact	Prof. Derek M Yellon, The Hatter Cardiovascular Institute, 0044 000, d.yellon@ucl.ac.uk
Scientific contact	Prof. Derek M Yellon, The Hatter Cardiovascular Institute, 0044 000, d.yellon@ucl.ac.uk

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	03 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2019
Global end of trial reached?	Yes
Global end of trial date	03 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. Does GTN administered as a continuous (intra-operative intravenous) infusion into a vein reduce injury to the heart muscle in patients undergoing heart-lung bypass Coronary Artery Bypass Graft (CABG) and/or valve surgery?

2. Does RIPC reduce injury to the heart muscle in the presence of GTN administered as a continuous (intra-operative intravenous) infusion into a vein in patients undergoing heart-lung bypass CABG and/or valve surgery?

Protection of trial subjects:

N/A

Background therapy:

GTN vs Placebo

Evidence for comparator: -

Actual start date of recruitment	01 July 2013
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	United Kingdom: 194
Worldwide total number of subjects	194
EEA total number of subjects	194

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)	57
From 65 to 84 years	112

85 years and over	25

Subject disposition

Recruitment

Recruitment details:

Patient assessment prior to their elective admission

Pre-assignment

Screening details:

Patient were screened prior to their elective admission using the elective cardiac surgery lists.

Period 1

Period 1 title	Full period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	RIP+Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

as per anesthetic team

Arm title	RIC+GTN

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	GTN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

As per anesthetic team

Arm title	Sham+GTN

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

as per anesthetic team

Investigational medicinal product name	GTN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:
As per anesthetics

Arm title	Sham+Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:
as per anesthetic team

Number of subjects in period 1	RIP+Placebo	RIC+GTN	Sham+GTN
Started	43	49	47
Completed	43	49	47

Number of subjects in period 1	Sham+Placebo
Started	45
Completed	45

Period 2

Period 2 title	baseline period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Arm title	Sham and GTN

Arm description: -

Arm type	Experimental

Investigational medicinal product name	GTN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

As per anesthetics

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: PERIOD 1 is the baseline period.

Number of subjects in period 2[2][3]	Sham and GTN
Started	47
Completed	47

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: these are consistent

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: This is due to drop outs and those who did not complete the trial.

Baseline characteristics

End points

End points reporting groups

Reporting group title	RIP+Placebo
Reporting group description: -	
Reporting group title	RIC+GTN
Reporting group description: -	
Reporting group title	Sham+GTN
Reporting group description: -	
Reporting group title	Sham+Placebo
Reporting group description: -	
Reporting group title	Sham and GTN
Reporting group description: -	

Primary: Area under the curve for mean troponin

End point title	Area under the curve for mean troponin[1]

End point description:

End point type	Primary

End point timeframe:

01/2013 - 01/2019

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: statistical analysis was undertaken

End point values	RIP+Placebo	RIC+GTN	Sham+GTN	Sham+Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	49	47	45
Units: tropinin level				
geometric mean (geometric coefficient of variation)				
GTN-Sham	28085 (± 0.8)	28085 (± 0.8)	28085 (± 0.8)	28085 (± 0.8)
GTN-RIPC	31933 (± 1.8)	31933 (± 1.8)	31933 (± 1.8)	31933 (± 1.8)
Placebo-sham	33775 (± 0)	33775 (± 0)	33775 (± 0)	33775 (± 0)
placebo-RIPC	17945 (± 0.6)	17945 (± 0.6)	17945 (± 0.6)	17945 (± 0.6)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

03/2013 - 06/2019

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	2.0

Reporting groups

Reporting group title	Adverse event

Reporting group description: -

Serious adverse events	Adverse event		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Adverse event		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 27 (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: Only SAEs occurred in the trial no non -serious adverse events

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2015	Adding substudy
20 August 2015	Removing 72H tropinin level from trial

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 April 2015	Moving trial to Barts Trust	09 September 2015

Notes:

Limitations and caveats

None reported