Clinical trial results:
Randomised Control Trial To Compare The Effects Of G-CSF And Autologous Bone Marrow Progenitor Cells Infusion On Quality Of Life And Left Ventricular Function In Patients With Heart Failure Secondary to Ischaemic Heart Disease- REGENERATE-IHD

Summary

EudraCT number	2005-002706-27
Trial protocol	GB
Global end of trial date	08 April 2015

Results information

Result version number	v1 (current)
This version publication date	09 September 2017
First version publication date	09 September 2017
Summary attachment (see zip file)	Regen IHD results (Regen IHD- result summary.pdf)

Trial information

Trial identification

Sponsor protocol code	Reda 005286

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00747708
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Jessry Veerapen, Barts Health NHS Trust, 44 2037658708, dj.veerapen@bartshealth.nhs.uk
Scientific contact	Prof Anthony Mathur, Queen Mary University, 44 2037658704, a.mathur@qmul.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	26 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether peripheral mobilisation of autologous stem cells and intracardiac administration of the mononuclear fraction of bone marrow derived cells will lead to an improvement in symptoms and cardiac function in patients with heart failure

Protection of trial subjects:

Data Protection Act

Data Safety Monitoring Committee

Background therapy:

Standard treatment for heart failure secondary to ischaemic heart disease as per National and European standards.

Evidence for comparator: -

Actual start date of recruitment	01 April 2005
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: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	54
From 65 to 84 years	36

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started in 2005 with the first patient consented in May 2005. The last patient was recruited in June 2011. A total of 90 patients successfully completed the trial assessments.

Pre-assignment

Screening details:

1133 patients were screened for eligibility, 105 consented but only 90 patients treated on the trial. 1028 patients were excluded and the breakdown is as follows: Normal LV EF n=236, Valvular disease n= 32, Non- ischaemic HF n=79, renal function n=24, RIP n=53, AF n=27, No ICF n=389, other co-morbidities n=188.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Randomisation was performed via a dedicated electronic software to either one of the 3 arms of the study (Peripheral, Intracoronary, Intramyocardial). Within each arm the patient was randomised to either the placebo or active arm. Participants, research team and analyst were blinded to whether patients received placebo or stem cell but not to which treatment arm they were assigned to.

Arms

Are arms mutually exclusive?	Yes
Arm title	Peripheral

Arm description:

30 patients randomised to the peripheral arm and were further assigned to either receive placebo or G-CSF. Patients were blinded to the which placebo/active arm but due to haematological response, the researchers would be able to determine the treatment arm they were assigned to.

Arm type	Placebo
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Arm title	Intracoronary

Arm description:

30 patients were randomised into this arm and further randomised in 1:1 ratio to stem cell versus placebo. Following G-CSF injection, patients underwent a bone marrow procedure. 15 patients were re-infused with stem cell and 15 patients were with serum placebo.

Arm type	Placebo
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Arm title	Intramyocardial

Arm description:

30 patients were randomised in this arm and further randomised in 1:1 ratio to either receive stem cell or placebo intramyocardial infusions.

Arm type	Placebo
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Arm title	Peripheral

Arm description:

30 patients randomised to the peripheral arm and were further assigned to either receive placebo or G-CSF. Patients were blinded to the which placebo/active arm but due to haematological response, the researchers would be able to determine the treatment arm they were assigned to.

Arm type	Active comparator
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Arm title	Intracoronary

Arm description:

30 patients were randomised into this arm and further randomised in 1:1 ratio to stem cell versus placebo. Following G-CSF injection, patients underwent a bone marrow procedure. 15 patients were re-infused with stem cell and 15 patients were with serum placebo.

Arm type	Active comparator
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Arm title	Intramyocardial

Arm description:

30 patients were randomised in this arm and further randomised in 1:1 ratio to either receive stem cell or placebo intramyocardial infusions.

Arm type	Active comparator
Investigational medicinal product name	Granocytes colony forming factor
Investigational medicinal product code	G-CSF
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

IMP was administered at 10ug/kg/day for days.

Number of subjects in period 1	Peripheral	Intracoronary	Intramyocardial
Started	15	15	15
Completed	15	15	15

Number of subjects in period 1	Peripheral	Intracoronary	Intramyocardial
Started	15	15	15
Completed	15	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
Patients with symptomatic ischaemic cardiomyopathy and no further treatment options were enrolled and randomised.	

Reporting group values	Overall trial	Total	
Number of subjects	90	90	
Age categorical			
Patient above 18 years of age and less or equal to 80 years.			
Units: Subjects			
18 years >Age <81 years	90	90	
Gender categorical			
5 out of 90 participants were female.			
Units: Subjects			
Female	5	5	
Male	85	85	

End points

End points reporting groups

Reporting group title	Peripheral
Reporting group description:	
30 patients randomised to the peripheral arm and were further assigned to either receive placebo or G-CSF. Patients were blinded to the which placebo/active arm but due to haematological response, the researchers would be able to determine the treatment arm they were assigned to.	
Reporting group title	Intracoronary
Reporting group description:	
30 patients were randomised into this arm and further randomised in 1:1 ratio to stem cell versus placebo. Following G-CSF injection, patients underwent a bone marrow procedure. 15 patients were re-infused with stem cell and 15 patients were with serum placebo.	
Reporting group title	Intramyocardial
Reporting group description:	
30 patients were randomised in this arm and further randomised in 1:1 ratio to either receive stem cell or placebo intramyocardial infusions.	
Reporting group title	Peripheral
Reporting group description:	
30 patients randomised to the peripheral arm and were further assigned to either receive placebo or G-CSF. Patients were blinded to the which placebo/active arm but due to haematological response, the researchers would be able to determine the treatment arm they were assigned to.	
Reporting group title	Intracoronary
Reporting group description:	
30 patients were randomised into this arm and further randomised in 1:1 ratio to stem cell versus placebo. Following G-CSF injection, patients underwent a bone marrow procedure. 15 patients were re-infused with stem cell and 15 patients were with serum placebo.	
Reporting group title	Intramyocardial
Reporting group description:	
30 patients were randomised in this arm and further randomised in 1:1 ratio to either receive stem cell or placebo intramyocardial infusions.	

Primary: Change in Left Ventricular Ejection Fraction

End point title	Change in Left Ventricular Ejection Fraction
End point description:	
Patient left ventricular ejection was assessed at baseline and at 12 month via advanced cardiac imaging, i.e. CT or CMR.	
End point type	Primary
End point timeframe:	
1 year	

End point values	Peripheral	Intracoronary	Intramyocardial	Peripheral
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	15	15
Units: percentage				
number (not applicable)	-0.98	1.1	4.15	-1.25

End point values	Intracoronary	Intramyocardial		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage				
number (not applicable)	0.89	4.99		

Statistical analyses

Statistical analysis title	Statistical design and analysis
Statistical analysis description:	
A paired T-test to detect any statistically significance of within-group change in LVEF	
Comparison groups	Peripheral v Intracoronary v Intramyocardial v Peripheral v Intracoronary v Intramyocardial
Number of subjects included in analysis	90
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.038
Method	Paired-T test
Parameter estimate	as above
Point estimate	4.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	9.6
Variability estimate	Standard deviation

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Adverse event were collected throughout the duration of each subject time on the trial.	
Adverse event reporting additional description:	
All events were recorded and reported.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

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

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: Due to ethics stipulation at the time of study approval, all events were reported were SAE.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2005	Changes to study criteria to exclude patients with positive virology, AF, does not respond to device, weight >143kg. Addition of pre-med and extra bone marrow sample to be taken for other research.
01 May 2008	Change to protocol to add cardiac CT for patients unable to undergo cardiac MRI.
05 November 2008	Addition of a thymosin bta-4 sub-study was added to explore the mechanism of action by which bone marrow derived stem cells improve cardiac functions.
14 October 2011	Addition of the angiogenesis study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported