Clinical trial results:
Evaluation of the feasibility of modulating and measuring endogenous neurogenesis with erythropoietin (rhEPO) to expedite recovery after stroke

Summary

EudraCT number	2011-000123-33
Trial protocol	GB
Global end of trial date	04 April 2014

Results information

Result version number	v1 (current)
This version publication date	26 October 2018
First version publication date	26 October 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (NIHR_EPO_RISC_final_report_28_10_14.pdf)

Trial information

Trial identification

Sponsor protocol code	RH EPOA-REHAB

Additional study identifiers

ISRCTN number	ISRCTN50896492
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College Hospital
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE5 9RS
Public contact	Professor Lalit Kalra, King's College Hospital NHS Foundation Trust, 0044 0203299 1718, lalit.kalra@kcl.ac.uk
Scientific contact	Professor Lalit Kalra, King's College Hospital NHS Foundation Trust, 0044 0203299 1718, lalit.kalra@kcl.ac.uk
Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor Lalit Kalra, King's College London, 0044 0203299 1718, lalit.kalra@kcl.ac.uk
Scientific contact	Professor Lalit Kalra, King's College London, 0044 0203299 1718, lalit.kalra@kcl.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	29 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2013
Global end of trial reached?	Yes
Global end of trial date	04 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Does treatment with erythropoetin (EPO) during post acute rehabilitation of non-thrombolysed patients improve functional recovery in stroke patients?

Can multimodal MR imaging be used for in vivo monitoring of brain repair in humans and do MRI parameters correlate with clinical measures of function recovery.

Protection of trial subjects:

The Data Monitoring Committee will review safety data, incidence of new thrombotic events and any cases where the Hb rises above the normal range. The data will be reviewed afte r10 patients have been recruited into each of the treatment arms, or 6 monthly intervals, whichever is sooner.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	13 November 2012
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: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

12 subjects were recruited however only 10 were eligible after baseline and only 3 subjects completed the protocol visits.

Pre-assignment

Screening details:

Baseline Assessment Within 48 Hours of Onset of Stroke
The following information will be collected prior to randomisation:
- Consent
– Medical history, stroke characteristics, vascular risk profile
– National Institute of Health Stroke Scale (NIHSS) score
– BP, temperature, heart rate
– Haemogram, renal and liver function tests
– CT findings

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Full study

Arm description:

The research design was to investigate 3 groups of 30 stroke patients each who were within 48 hours of stroke onset, had not been thrombolysed and had no contraindications to rhEPOα treatment. All groups received the best usual treatment consisting of structured multidisciplinary rehabilitation on a stroke unit. In addition, participants in the second group received rh EPOα alfa (Eprex) 40,000 IU given intravenously at 1, 3 and 5 days and those in the third group will receive rh EPOα 40,000 IU/ given intravenously at 7, 14, 21 days. The differences in recovery between the groups was assessed at 30 and 90 days after randomisation by measuring clinical recovery in function and changes in the brain perfusion and structure using magnetic resonance (MR) imaging.

Arm type	Experimental
Investigational medicinal product name	EPREX 40,000 IU/ml, solution for injection in pre-filled syringe
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Each patient will receive epoetin alfa (EPREX) 40,000 IU given intravenously over 5-10 minutes at 1, 3 and 5 days or 7, 14 and 21 days post
randomization.

Number of subjects in period 1	Full study
Started	12
Completed	3
Not completed	9
Consent withdrawn by subject	7
ineligable	2

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	5	
Male	7	7	

End points

End points reporting groups

Reporting group title	Full study

Reporting group description:

The research design was to investigate 3 groups of 30 stroke patients each who were within 48 hours of stroke onset, had not been thrombolysed and had no contraindications to rhEPOα treatment. All groups received the best usual treatment consisting of structured multidisciplinary rehabilitation on a stroke unit. In addition, participants in the second group received rh EPOα alfa (Eprex) 40,000 IU given intravenously at 1, 3 and 5 days and those in the third group will receive rh EPOα 40,000 IU/ given intravenously at 7, 14, 21 days. The differences in recovery between the groups was assessed at 30 and 90 days after randomisation by measuring clinical recovery in function and changes in the brain perfusion and structure using magnetic resonance (MR) imaging.

Primary: Clinical Endpoint

End point title	Clinical Endpoint[1]

End point description:

– Fugl-Meyer scale score
– Fugl-Meyer scale score change from baseline

End point type	Primary

End point timeframe:

Clinical outcome measures will be assessed at baseline, 30 ± 5 days and 90 ±10 days after randomisation.

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: The findings would not be significant as the number of participants at the close of the study was well below the numbers needed to be statistically significant. Only 3 participants completed the trial.

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: whole	3			

Attachments (see zip file)	EPO-REHAB tables/Results Tables.docx

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Endpoint

End point title	Clinical Endpoint

End point description:

Secondary clinical outcome measures were the NIHSS score, Functional Independence Measure (FIM), FIM Motor score, Modified Rankin score (MRS) and Mortality

End point type	Secondary

End point timeframe:

Baseline and 30 days post dose.

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: whole	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Imaging

End point title	Imaging

End point description:

Evaluate whether MRI techniques can be used for in vivo imaging of brain repair in humans and correlate MRI parameters with clinical measures of function recovery

End point type	Secondary

End point timeframe:

90 days post dose

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: whole	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Throughout the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Whole Trial

Reporting group description: -

Serious adverse events	Whole Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (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 %

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (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: No adverse events were recorded due to the very small final dataset.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2011	Changes to MHRA-approved protocol , including inclusion/exclusion, following REC review

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 findings would not be significant as the number of participants at the close of the study was well below the numbers needed to be statistically significant. Only 3 participants completed the trial.

Notes: