

**Clinical trial results:****Elafin Myocardial Protection from Ischaemia RepErfusion injury: A randomised trial to investigate the effect of Elafin on myocardial injury and inflammation in coronary bypass surgery (EMPIRE)****Summary**

EudraCT number	2010-019527-58
Trial protocol	GB
Global end of trial date	16 November 2013

**Results information**

Result version number	v1 (current)
This version publication date	01 August 2020
First version publication date	01 August 2020
Summary attachment (see zip file)	Perioperative elafin for ischaemia-reperfusion injury during coronary artery bypass graft surgery: a randomised-controlled trial (1639.full.pdf)

**Trial information****Trial identification**

Sponsor protocol code	2010-019527-58
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**Additional study identifiers**

ISRCTN number	ISRCTN82061264
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	ACCORD (University of Edinburgh & NHS Lothian)
Sponsor organisation address	47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
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Scientific contact	Dr Peter Henriksen, University of Edinburgh, +44 0131 537 3834, phenrik1@staffmail.ed.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	14 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2013
Global end of trial reached?	Yes
Global end of trial date	16 November 2013
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that perioperative Elafin administration reduces post-ischaemic inflammatory myocardial injury following coronary artery bypass graft surgery.

Protection of trial subjects:

This single center clinical trial was performed with the approval of the national research ethics committee (11/MRE00/5), in accordance with the Declaration of Helsinki (2000), under a Clinical Trial Authorization (27586/0015/001-0001) from the Medicine and Healthcare products Regulatory Authority (MHRA, United Kingdom), and the written informed consent of all participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 August 2011
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: 87
Worldwide total number of subjects	87
EEA total number of subjects	87

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)	47
From 65 to 84 years	40



## Subject disposition

### Recruitment

Recruitment details:

Between June 2011 and September 2013, consecutive patients referred for elective CABG surgery were recruited from two clinics at Edinburgh Heart Centre. Patients were 18 years or older, and were referred for isolated CABG surgery requiring 2 or more grafts. Exclusion criteria included patients with recent myocardial infarction (within 1 month of su

### Pre-assignment

Screening details:

A total of 189 patients were screened for recruitment of whom 29 were excluded, 79 declined to participate, 88 patients gave informed consent and 1 died before surgery leaving 87 patients to undergo randomisation.

### 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, Assessor

Blinding implementation details:

Treatment was blinded to both the research team and the subject. To ensure blinding, study drugs were prepared by staff independent of the study investigators or clinical team responsible for the patients care.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Active

Arm description:

Elafin

Arm type	Experimental
Investigational medicinal product name	Elafin
Investigational medicinal product code	CAS number: 820211-82-3.
Other name	N/A
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous recombinant human Elafin (Proteo Biotech AG, Germany) 200 mg was prepared and infused as aqueous solution of 250 mL 0.9% saline.

<b>Arm title</b>	Placebo
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Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	0.9% saline
Investigational medicinal product code	
Other name	N/A
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Saline placebo was prepared and infused as aqueous solution of 250 mL 0.9% saline.

<b>Number of subjects in period 1</b>	Active	Placebo
Started	44	43
Received infusion	43	42
Completed	43	42
Not completed	1	1
Infusion not given - not informed of surgery time	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	Active
Reporting group description: Elafin	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Active	Placebo	Total
Number of subjects	44	43	87
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	24	23	47
From 65-84 years	20	20	40
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	63.9	63.6	
standard deviation	± 7.7	± 8.4	-
Gender categorical			
Units: Subjects			
Female	6	7	13
Male	38	36	74
Baseline Data - characteristics used in minimisation algorithm (Diabetes mellitus)			
Characteristics used in minimisation algorithm			
Units: Subjects			
Diabetes mellitus present	11	9	20
Diabetes mellitus absent	33	34	67
Baseline data - characteristics used in minimisation algorithm (extent of coronary artery disease)			
Characteristics used in minimisation algorithm			
Units: Subjects			
2 vessel	11	12	23
3 vessel	33	31	64
Baseline data - characteristics used in minimisation algorithm (eGFR (mL/min))			
Characteristics used in minimisation algorithm			

Units: Subjects			
40 to 60	5	4	9
60+	39	39	78
Baseline data - characteristics used in minimisation algorithm (surgeon)			
Characteristics used in minimisation algorithm			
Units: Subjects			
Surgeon A	18	16	34
Surgeon B	26	27	53

## End points

### End points reporting groups

Reporting group title	Active
Reporting group description:	Elafin
Reporting group title	Placebo
Reporting group description:	Placebo

### Primary: The primary endpoint is the log area under the curve for plasma troponin I concentration profile over the first 48 h

End point title	The primary endpoint is the log area under the curve for plasma troponin I concentration profile over the first 48 h
End point description:	
End point type	Primary
End point timeframe:	48 hours

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42 <sup>[1]</sup>	41 <sup>[2]</sup>		
Units: unitless				
arithmetic mean (standard deviation)	4.44 ( $\pm$ 1)	4.77 ( $\pm$ 1.1)		

Notes:

[1] - 2 patients AUC could not be calculated - no Troponin I blood result/ highly-sensitive Troponin value

[2] - 2 patients AUC could not be calculated - no Troponin I blood result/ highly-sensitive Troponin value

### Statistical analyses

Statistical analysis title	48 hour plasma troponin I concentration profile
Statistical analysis description:	Log area under the curve for plasma troponin I concentration profile over the first 48 h. General linear model.
Comparison groups	Active v Placebo
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181 <sup>[3]</sup>
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.3

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Confidence interval

level	95 %
sides	2-sided
lower limit	-0.75
upper limit	0.14

Notes:

[3] -  $P=0.05$

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) that occur after joining the trial must be reported in detail in the CRF. In the case of an AE, the Investigator should initiate the appropriate treatment according to their medical judgement. Participants with AEs present at the

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

### Reporting groups

Reporting group title	Active
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Reporting group description:

Elafin

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	No treatment received
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Reporting group description:

Participants were consented but had received no treatment at the time of adverse event

<b>Serious adverse events</b>	Active	Placebo	No treatment received
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 43 (9.30%)	5 / 42 (11.90%)	2 / 3 (66.67%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Surgery			
subjects affected / exposed	4 / 43 (9.30%)	5 / 42 (11.90%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Active	Placebo	No treatment received
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 43 (60.47%)	18 / 42 (42.86%)	0 / 3 (0.00%)
Surgical and medical procedures			

Surgery subjects affected / exposed occurrences (all)	26 / 43 (60.47%) 26	18 / 42 (42.86%) 18	0 / 3 (0.00%) 0
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## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2011	Removing women of child bearing potential. Protocol v3
16 June 2011	Detailing the delay in supply of feraheme but adding text to protocol and PIS to allow start of recruitment without this aspect of study. Protocol v5
21 March 2012	Extension of shelf life. Protocol v7
05 September 2012	Addition of 10 healthy volunteers. Protocol v8
10 April 2013	Extension request and addition of 36 additional participants without MRI scans. Protocol v9

Notes:

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### 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.

N/A

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26310261>