Clinical trial results:
MINeralocorticoid receptor antagonist pretreatment to MINIMISE reperfusion injury after ST-Elevation Myocardial Infarction(STEMI).

Summary

EudraCT number	2013-001069-18
Trial protocol	GB
Global end of trial date	04 April 2016

Results information

Result version number	v1 (current)
This version publication date	24 August 2017
First version publication date	24 August 2017
Summary attachment (see zip file)	Trial design paper (MINIMISE-STEMI Trial design paper.pdf)

Trial information

Trial identification

Sponsor protocol code	12/0533

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT number: 2013-001069-18

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	149 Tottenham Court Road, London, United Kingdom, London W1T 7DN
Public contact	Derek Hausenloy, Hatter Cardiovascular Institute, +44 203 447 9894, d.hausenloy@ucl.ac.uk
Scientific contact	Derek Hausenloy, Hatter Cardiovascular Institute, +44 203 447 9894, d.hausenloy@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	06 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2016
Global end of trial reached?	Yes
Global end of trial date	04 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Does the administration of mineralo-corticoid-receptor antagonist (MRA) therapy initiated prior to coronary angioplasty followed by three months MRA therapy reduced the damage to the heart muscle in patients presenting with a heart attack?

Protection of trial subjects:

No applicable

Background therapy: -

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: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	42
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

111 patients gave initial consent and 70 patients were enrolled in the study.

Pre-assignment

Screening details:

951 patients were screened between November 2013 and January 2016

Period 1

Period 1 title	Nov 2013 to Jan 2016 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

Eligible patients were randomised by the unblinded study investigator to Aldactone® canrenoate treatment or placebo immediately after the diagnostic coronary angiography. Randomisation was done on a web-based service through www.SealedEnvelope.com. The study team member collecting the data at each study site remained blinded to the allocation of patients to either intervention or placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention arm

Arm description:

one single bolus i.v. Aldactone® canrenoate 200 mg prior to reopening of the infarcted artery followed by 25 mg spironolactone oral, daily for 3 months.

Arm type	Experimental
Investigational medicinal product name	Aldactone canrenoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Aldactone® canrenoate 200 mg prior to reopening of the infarcted artery followed by 3 months of oral spironolactone 25 mg

Arm title	Placebo

Arm description:

10 ml normal saline drawn-up into an identical opaque syringe given as a bolus over 2 minutes.

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

Dosage and administration details:

The placebo was 10 ml normal saline drawn-up into an identical opaquesyringe given as a bolus over 2 minutes, prior to PPCI

Number of subjects in period 1	Intervention arm	Placebo
Started	38	32
Interim analysis	38	32
Completed	38	32

Baseline characteristics

Reporting groups

Reporting group title	Nov 2013 to Jan 2016

Reporting group description: -

Reporting group values	Nov 2013 to Jan 2016	Total	
Number of subjects	70	70	
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)	42	42	
From 65-84 years	28	28	
85 years and over	0	0	
Age continuous Units: years			
median	62		
inter-quartile range (Q1-Q3)	53 to 69	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	60	60	

End points

End points reporting groups

Reporting group title	Intervention arm

Reporting group description:

one single bolus i.v. Aldactone® canrenoate 200 mg prior to reopening of the infarcted artery followed by 25 mg spironolactone oral, daily for 3 months.

Reporting group title	Placebo

Reporting group description:

10 ml normal saline drawn-up into an identical opaque syringe given as a bolus over 2 minutes.

Primary: Chronic infarct size by CMR

End point title	Chronic infarct size by CMR

End point description:

End point type	Primary

End point timeframe:

3 months

End point values	Intervention arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	32		
Units: percentage				
arithmetic mean (standard deviation)	16 (± 10)	17 (± 11)		

Statistical analyses

Statistical analysis title	Primary outcome analysis

Statistical analysis description:

The primary endpoint (myocardial infarct (MI) size in grams at 12 weeks) was compared between those randomised to placebo and those randomised to mineralocorticoid receptor antagonist therapy (MRA) using linear regression with the myocardial infarct size at three months as the response variable and the treatment group included as a binary covariate in the model. The distribution of MI size in grams showed marked positive skew, but this distribution was normalised by expressing MI size as % of LV

Comparison groups	Placebo v Intervention arm
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (net)

Secondary: Acute MI size by CMR

End point title	Acute MI size by CMR

End point description:

End point type	Secondary

End point timeframe:

Within the first week.

End point values	Intervention arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	32		
Units: percentage				
arithmetic mean (standard deviation)	23 (± 14)	26 (± 16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Microvascular obstruction

End point title	Microvascular obstruction

End point description:

End point type	Secondary

End point timeframe:

One week

End point values	Intervention arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	32		
Units: percentage	65	67		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in end-diastolic volume at 3 months

End point title	Change in end-diastolic volume at 3 months
End point description: Change in LV end-diastolic at 3 months	
End point type	Secondary
End point timeframe: 3 months	

End point values	Intervention arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	32		
Units: percentage				
arithmetic mean (standard deviation)	-3 (± 16)	10 (± 14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in end-systolic volume at 3 months

End point title	Change in end-systolic volume at 3 months
End point description: Cchange in end-systolic volume at 3 months	
End point type	Secondary
End point timeframe: 3 months	

End point values	Intervention arm	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	32		
Units: percentage				
arithmetic mean (standard deviation)	-12 (± 24)	6 (± 24)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: November 2015 to April 2016	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Intervention
Reporting group description: -	

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: Less than 5% of non-serious adverse events recorded.

Serious adverse events	Placebo	Intervention	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 32 (28.13%)	11 / 38 (28.95%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Chest pain			
subjects affected / exposed	3 / 32 (9.38%)	5 / 38 (13.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arrhythmia			
subjects affected / exposed	4 / 32 (12.50%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Panic attack			
subjects affected / exposed	1 / 32 (3.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 32 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 32 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 32 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Intervention	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 38 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2016	Change in trial statistician which led to a change in statistical plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported