Clinical trial results:
The Effect of Sildenafil (REVATIO®) on Post Cardiac Surgery Acute Kidney Injury: A Randomised, Placebo-controlled Phase IIb Clinical Trial: The REVAKI-2 Trial

Summary

EudraCT number	2015-003259-24
Trial protocol	GB
Global end of trial date	20 September 2018

Results information

Result version number	v1 (current)
This version publication date	26 October 2019
First version publication date	26 October 2019
Summary attachment (see zip file)	Study Manuscript (proof) (REVAKI-2 PDF Proof.pdf)

Trial information

Trial identification

Sponsor protocol code	0360

Additional study identifiers

ISRCTN number	ISRCTN18386427
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Leicester
Sponsor organisation address	University Road, Leicester, United Kingdom,
Public contact	Research Manager, Mrs Tracy Kumar, 44 01162583039, tk98@le.ac.uk
Scientific contact	Research Manager, Mrs Tracy Kumar, 44 01162583039, tk98@le.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	18 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 September 2018
Global end of trial reached?	Yes
Global end of trial date	20 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The REVAKI-2 Trial proposes to test the hypothesis that postoperative acute kidney injury (AKI) will be less in cardiac surgery patients identified as being at increased risk of developing AKI preoperatively, by the administration of sildenafil, a PDE-5 inhibitor

Protection of trial subjects:

Exclusion criteria applied regarding contra-indication for the investigation product.

Research bloods attempted to be taken at the same time as routine clinical blood tests to minimise risk of pain, bruising, blood clots, and infections.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 129
Worldwide total number of subjects	129
EEA total number of subjects	129

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)	0
From 65 to 84 years	125
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

There were 129 patients recruited and randomised between September 2015 and September 2018 which made up the analysis population, 60 of whom were allocated to Sildenafil and 69 to Placebo.

Pre-assignment

Screening details:

Potential research participants were identified by qualified study staff from clinical and theatre lists and hospital medical notes and referrals from other trusts.

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

Blinding implementation details:

The active drug or placebo according to randomisation will be prepared by the unblinded researchers. This will be prepared in a clinical area whereby the unblinded researchers are the only team members aware of the allocated treatment. The blinded team will not handle the supply or returns of the investigational medicinal product. Both active drug (bolus and infusion) and placebo (bolus and infusion) will be clearly labelled as REVAKI-2 sildenafil/placebo and are identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sildenafil

Arm description:

Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously over 150 minutes starting at the time of skin incision.

Arm type	Experimental
Investigational medicinal product name	Sildenafil Citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously over 150 minutes starting at the time of skin incision.

Arm title	Placebo

Arm description:

. In the Placebo group, a 5% dextrose solution was administered to the same volume and timing as the intervention (Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously over 150 minutes starting at the time of skin incision).

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

Dosage and administration details:

. In the Placebo group, a 5% dextrose solution was administered to the same volume and timing as the intervention (Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously

over 150 minutes starting at the time of skin incision.)

Number of subjects in period 1	Sildenafil	Placebo
Started	60	69
Completed	55	62
Not completed	5	7
Adverse event, serious fatal	1	3
Lost to follow-up	4	4

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	129	129	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	72		
full range (min-max)	52 to 88	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	105	105	

End points

End points reporting groups

Reporting group title	Sildenafil

Reporting group description:

Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously over 150 minutes starting at the time of skin incision.

Reporting group title	Placebo

Reporting group description:

. In the Placebo group, a 5% dextrose solution was administered to the same volume and timing as the intervention (Sildenafil citrate 12.5mg in 65mls of 5% dextrose solution was administered intravenously over 150 minutes starting at the time of skin incision).

Primary: Serum Creatinine

End point title	Serum Creatinine[1][2]

End point description:

End point type	Primary

End point timeframe:

pre-operation to 96 hours post-surgery

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: Please see manuscript attachment

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see manuscript attachment

End point values	Sildenafil			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: µmol.L-1				
number (confidence interval 95%)	0.88 (-5.82 to 7.59)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: consent to 3 month follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14

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

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: Please see manuscript attachment

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2016	List of expected adverse events was updated. Concomitant medication timing was updated
13 June 2017	The AKI risk score used in the inclusion criteria was amended. The blood volumes to be collected were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported