Clinical trial results:
Effect of hypertonic saline solute compared to ringer lactate on right ventricular function after cardiac surgery

Summary

EudraCT number	2015-004485-28
Trial protocol	FR
Global end of trial date	24 August 2018

Results information

Result version number	v1 (current)
This version publication date	25 May 2022
First version publication date	25 May 2022

Trial information

Trial identification

Sponsor protocol code	38RC15.214

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Grenoble University Hospital
Sponsor organisation address	CS 10217 , Grenoble, France, 38043
Public contact	Dr Michel DURAND, Centre Hospitalier Universitaire, 33 04 76 76 55 10 , MDurand@chu-grenoble.fr
Scientific contact	Dr Michel DURAND, Centre Hospitalier Universitaire, 33 04 76 76 55 10 , MDurand@chu-grenoble.fr

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	24 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2017
Global end of trial reached?	Yes
Global end of trial date	24 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was right ventricular function improvement after hypertonic saline solution infusion compared to an isotonic solution

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements including relative provisions to biomedical research of "Code de la santé publique" . The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice.
The protocol has been authorized by the "Comité de Protection des personnes Sud Est" and the "Agence nationale de sécurité du medicament".

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	13
From 65 to 84 years	17

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients undergoing cardicac surgery (valvular replacement, coronary bypass surgery or ascending aorta surgery) in the CHU de Grenoble. Patients had to be in sinus rhythm, and have an indication for swan Ganz catheter.

Pre-assignment

Screening details:

The recruitment will be done in patients who will undergo cardiac surgery for coronary bypass or valvulopathy in the cardiac surgery department of the University Hospital of Grenoble.

Pre-assignment period milestones

Number of subjects started	30
Number of subjects completed	30

Period 1

Period 1 title	hypertonic saline sol 7.5/Ringer lactate (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Hypertonic Saline Solution

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Hypertonic Saline Solution (HSS) 7.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

3 mL/kg

Arm title	Ringer Lactate

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ringer Lactate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mL/kg

Number of subjects in period 1	Hypertonic Saline Solution	Ringer Lactate
Started	15	15
Completed	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Hypertonic Saline Solution
Reporting group description: -	
Reporting group title	Ringer Lactate
Reporting group description: -	

Reporting group values	Hypertonic Saline Solution	Ringer Lactate	Total
Number of subjects	15	15	30
Age categorical Units: Subjects			
Adults (18-64 years)	7	6	13
From 65-84 years	8	9	17
Gender categorical Units: Subjects			
Female	12	12	24
Male	3	3	6

End points

End points reporting groups

Reporting group title	Hypertonic Saline Solution
Reporting group description: -	
Reporting group title	Ringer Lactate
Reporting group description: -	

Primary: Evolution of right ventricular ejection fraction (RVEF) 30 minutes after volume expansion of a filling solution in the two arm groups.

End point title	Evolution of right ventricular ejection fraction (RVEF) 30 minutes after volume expansion of a filling solution in the two arm groups.
End point description:	
End point type	Primary
End point timeframe:	
30 minutes after volume expansion of a filling solution in the two arm groups.	

End point values	Hypertonic Saline Solution	Ringer Lactate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage				
median (inter-quartile range (Q1-Q3))	35 (26 to 41)	28 (23 to 33)		

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description:	
Primary analysis A Student's t test will be performed for the comparison of FEVD in the two groups. It will be replaced by the non-parametric Mann-Whitney test when the normality or homogeneity of variances has been rejected	
Comparison groups	Hypertonic Saline Solution v Ringer Lactate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - End point values:
- Arm 1: 35
- Arm 2: 28

Secondary: Explore improvement in left ventricular function (LVEF)

End point title	Explore improvement in left ventricular function (LVEF)

End point description:

End point type	Secondary

End point timeframe:

30, 60 minutes and 3, 6 and 18 hours after infusion

End point values	Hypertonic Saline Solution	Ringer Lactate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[2]	15[3]		
Units: dp/DT / VS				
geometric mean (geometric coefficient of variation)	24 (± 0.44)	24.5 (± 0.07)		

Notes:

[2] - end point value: 24

[3] - end point value: 24.5

Statistical analyses

Statistical analysis title	Explore improvement in left ventricular function

Statistical analysis description:

Explore improvement in left ventricular function (LVEF)

Comparison groups	Hypertonic Saline Solution v Ringer Lactate
Number of subjects included in analysis	30
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.44 [4]
Method	ANOVA

Notes:

[4] - P-value: 0.44 / 0.07

Secondary: Demonstrate improvement in microcirculation

End point title	Demonstrate improvement in microcirculation

End point description:

Countable units : continuous cardiac output, venous oxygen saturation, and mean arterial pressure, in the hours following infusion at 30, 60 minutes and 3, 6, and 18 hours post-infusion.

End point type	Secondary

End point timeframe:

30, 60 minutes and 3, 6, and 18 hours post-infusion.

End point values	Hypertonic Saline Solution	Ringer Lactate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[5]	15[6]		
Units: continuous cardiac output	66	68		

Notes:

[5] - end point values: 1.7 / 67.5 / 66

[6] - 1.6 / 62.4 / 68.5

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Hypertonic Saline Solution v Ringer Lactate
Number of subjects included in analysis	30
Analysis specification	Post-hoc
Analysis type	superiority[7]
P-value	= 0.13
Method	ANOVA

Notes:

[7] - End point values arm 2: 1.6 / 62.4 / 68.5

Secondary: Explore volumetric efficiency

End point title	Explore volumetric efficiency

End point description:

Systolic and diastolic right ventricular volumes measured by Swan Ganz, central venous pressure in the hour before filling and at 30, 60 minutes and 3, 6 and 18 hours after filling.

End point type	Secondary

End point timeframe:

1, 6, 18 hours after infusion

End point values	Hypertonic Saline Solution	Ringer Lactate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: ventricular vol, central venous pressure	109	89		

Statistical analyses

Statistical analysis title	secondary analysis
Comparison groups	Hypertonic Saline Solution v Ringer Lactate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3 [8]
Method	ANOVA

Notes:
[8] - 0.3 / 0.8 / 0.6

Secondary: explore tolerance to hypertonic saline

End point title	explore tolerance to hypertonic saline
End point description: Countable units : measurement of natraemia, and lactatemia at 1, 6, 18 hours after infusion	
End point type	Secondary
End point timeframe: 1, 6, 18 hours after infusion	

End point values	Hypertonic Saline Solution	Ringer Lactate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: natraemia and lactatemia	137	138		

Statistical analyses

Statistical analysis title	secondary analysis
Comparison groups	Ringer Lactate v Hypertonic Saline Solution
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: throughout the study	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1
Reporting groups	
Reporting group title	ventricular tachycardia

Reporting group description: -

Serious adverse events	ventricular tachycardia		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	ventricular tachycardia		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)		
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	30		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2017	Update of the BI and DME of sodium chloride APHP 7.5% following a batch change.
19 May 2017	Extension of the inclusion period by 1 year until June 2018 Update of the vigilance part

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported