Clinical trial results:
CUstodiol vs RInger: whaT Is the Best Agent?

Summary

EudraCT number	2014-003818-92
Trial protocol	IT
Global end of trial date	17 January 2018

Results information

Result version number	v1 (current)
This version publication date	29 May 2021
First version publication date	29 May 2021

Trial information

Trial identification

Sponsor protocol code	CURITIBA-TRIAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02327611
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20133
Public contact	UO Chirurgia Vascolare, IRCCS Ospedale San Raffaele, 0039 0226437377,
Scientific contact	UO Chirurgia Vascolare, IRCCS Ospedale San Raffaele, 0039 0226437377,

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	17 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2018
Global end of trial reached?	Yes
Global end of trial date	17 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the efficacy of renal perfusion with Custodiol versus enriched Ringer's solution for renal protection in patients undergoing open thoracoabdominal aortic aneurysm (TAAA) repair

Protection of trial subjects:

Approval by the local Ethics Committee was obtained before the beginning of the study and written informed consent was obtained from all patients at time of enrolment. Patients care was carried out by a multidisciplinary team.
Except for the solutions used during the perfusion, the trial did not affect any other aspect of patient treatment, which was left to standard clinical practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 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	Italy: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	30
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This prospective, single-center, randomized, double-blind, controlled, parallel trial involved 90 adult patients who were to undergo TAAA open repair surgery requiring renal perfusion. Patients were enrolled between February 2015 and january 2017. One year of follow up was completed in January 2018.

Pre-assignment

Screening details:

Patients who have participated in experimental trials during the previous 3 months, undergoing emergency/urgency intervention, patient uncooperative and/or affected by mental disease, with allergy/intolerance to the study drug, patient receiving chronic dialysis before surgery, and pregnant or breastfeeding women were excluded

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, Carer, Assessor

Blinding implementation details:

A computer-generated permuted block (up to a size of 10 and a 1:1 allocation) randomization sequence was used. Treatment allocation was prepared by an independent operator not otherwise involved in the trial. The patient was randomized upon operative room arrival by a CURITIBA trial staff member who prepared the blinded treatment and was not in any way involved in the clinical management of the patient. Both solutions are colorless, thus impossible to distinguish.

Arms

Are arms mutually exclusive?	Yes
Arm title	Custodiol Renal Perfusion

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Custodiol
Investigational medicinal product code	
Other name	Custodiol HTK, Histidine-tryptophan-ketoglutarate
Pharmaceutical forms	Solution for organ preservation
Routes of administration	Intraarterial use

Dosage and administration details:

Patients randomized in the Custodiol arm received, upon renal artery clamping, a renal perfusion with cold (4°C) Custodiol.
During renal ischemic time, a total of 1.5 mL of Custodiol per gram of estimated kidney weight were administered, thus implying an average of 400 mL of Custodiol for a 70-kg patient

Arm title	Ringer Renal Perfusion

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ringer's lactate
Investigational medicinal product code	
Other name	Lactated Ringer's solution, Sodium lactate solution
Pharmaceutical forms	Solution for infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Patients randomized in the enriched Ringer’s lactate arm received a renal perfusion with cold (4C) Ringer’s lactate solution enriched with 125 mg per liter of methylprednisolone and 12.5 g per liter of mannitol.

Number of subjects in period 1	Custodiol Renal Perfusion	Ringer Renal Perfusion
Started	45	45
Completed	44	44
Not completed	1	1
Intraoperative clinical reasons	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Custodiol Renal Perfusion
Reporting group description: -	
Reporting group title	Ringer Renal Perfusion
Reporting group description: -	

Reporting group values	Custodiol Renal Perfusion	Ringer Renal Perfusion	Total
Number of subjects	45	45	90
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 63.7 ± 9.82	 66.4 ± 9.21	 -
Gender categorical Units: Subjects			
Female	33	29	62
Male	12	16	28

End points

End points reporting groups

Reporting group title	Custodiol Renal Perfusion
Reporting group description: -	
Reporting group title	Ringer Renal Perfusion
Reporting group description: -	

Primary: Reduction of Acute renal failure (AKI)

End point title	Reduction of Acute renal failure (AKI)
End point description:	
Make a significant reduction of acute renal failure (AKI - Defined according to the diagram 2013.9 KDIGO) in postoperative surgical patients who receive renal perfusion with Custodiol vs standard perfusion with Ringer's lactate solution	
End point type	Primary
End point timeframe:	
28 days after surgery	

End point values	Custodiol Renal Perfusion	Ringer Renal Perfusion		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: number of patients				
Any AKI (AKIN 1 + 2+ 3)	22	34		
AKIN stage 0	23	11		
AKIN stage 1	11	18		
AKIN stage 2	7	7		
AKIN stage 3	4	9		
Severe AKI (AKIN 2 +3)	11	16		

Statistical analyses

Statistical analysis title	AKI Intention-to-treat analysis
Comparison groups	Custodiol Renal Perfusion v Ringer Renal Perfusion
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Lenght of stay in the Intensive care Unit (ICU)

End point title	Lenght of stay in the Intensive care Unit (ICU)

End point description:

End point type	Secondary

End point timeframe:

60 days after surgery

End point values	Custodiol Renal Perfusion	Ringer Renal Perfusion		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: day				
median (inter-quartile range (Q1-Q3))	1 (1 to 2)	1 (1 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lenght of hospitalyzation

End point title	Lenght of hospitalyzation

End point description:

End point type	Secondary

End point timeframe:

60 days after surgery

End point values	Custodiol Renal Perfusion	Ringer Renal Perfusion		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: day				
median (inter-quartile range (Q1-Q3))	15 (13 to 20)	15 (13 to 18)		

Statistical analyses

No statistical analyses for this end point

Secondary: In-hospital mortality

End point title	In-hospital mortality

End point description:

End point type	Secondary

End point timeframe:

During hospitalization

End point values	Custodiol Renal Perfusion	Ringer Renal Perfusion		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: number of patients	4	6		

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year survival

End point title	1-year survival

End point description:

End point type	Secondary

End point timeframe:

1 year after surgery

End point values	Custodiol Renal Perfusion	Ringer Renal Perfusion		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: percent				
number (confidence interval 95%)	91.1 (83 to 99)	84.4 (74 to 95)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Until the end of the annual follow-up	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Custodiol Renal Perfusion
Reporting group description: -	
Reporting group title	Ringer Renal Perfusion
Reporting group description: -	

Serious adverse events	Custodiol Renal Perfusion	Ringer Renal Perfusion	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	
number of deaths (all causes)	5	6	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Custodiol Renal Perfusion	Ringer Renal Perfusion	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (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 non-serious adverse event associated to the IMPs were recorded

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2015	Changes and clarifications regarding the randomization procedure Changes to some study procedures (e.g. sample collection, markers analysis, data recording)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24377947