Clinical trial results:
Influence of albumin on the development of acute renal dysfunction associated with cardiac surgery under extracorporeal circulation

Summary

EudraCT number	2017-003027-30
Trial protocol	ES
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	06 June 2022
First version publication date	06 June 2022

Trial information

Trial identification

Sponsor protocol code	IIBSP-ALB-2017-72

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut de Recerca Hospital de la Santa Creu i Sant Pau
Sponsor organisation address	Carrer de Sant Quintí, 77, Barcelona, Spain, 08041
Public contact	UICEC Sant Pau, Institut de Recerca Hospital de la Santa Creu i Sant Pau, 34 935537636, uicec@santpau.cat
Scientific contact	UICEC Sant Pau, Institut de Recerca Hospital de la Santa Creu i Sant Pau, 34 935537636, uicec@santpau.cat

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	29 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2019
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To analyze the effect of the use of human albumin during ECC on the incidence of ARD-ACC in patients undergoing cardiac surgery with CPB diagnosed according to the KDIGO scale during the first 7 days after the intervention.

Protection of trial subjects:

The study will be conducted in strict accordance with international ethical recommendations for research and clinical trials in humans. Likewise, the standards contained in the Declaration of Helsinki will be guaranteed and will be developed in accordance with the protocol and with the standard work procedures (SOPs) that ensure compliance with the standards of Good Clinical Practice (PCB).
The investigator should explain to the patient (when possible) or his authorized legal representative, the nature of the study, its purposes, procedures, estimated duration, the potential risks and benefits related to the participation in the study, as well as any inconvenience that this may cause. can suppose. Each of the participants should be warned that their participation in the study is voluntary and that they can leave the study at any time, without this affecting their subsequent treatment or their relationship with the professionals who treat them.
For this, an information / consent sheet has been designed for the patient or the authorized legal representative, which is attached.
Human albumin is currently used routinely in certain centers for priming the CEC circuit during cardiac surgery, its beneficial effect has been demonstrated in many respects, but its effect on renal function during the immediate postoperative period has not been evaluated. . The use of albumin in this context has shown benefits in terms of reducing postoperative bleeding, less need for fluid therapy, improved plasma oncotic pressure, as well as decreased formation of microthrombi, improved perfusion during circulation extracorporeal, decreased levels of nephrotoxic free radicals released during extracorporeal circulation and other effects that may be protective factors of kidney function during the period of extracorporeal circulation.
Monitoring, audits, CEIC reviews and regulatory inspections related to the test will be allowed, facilitating direct access to the original documents / data.

Background therapy:

Albumin in cardiac surgery
Albumin is a 66 kD protein synthesized in the liver, which is responsible for 75 to 80% of plasma oncotic pressure, with a half-life of around 20 days [19], being of high importance for proper function of the vascular barrier and the integrity of the glycocalix, bases of vascular permeability and homeostasis of the intracellular and interstitial spaces, in which albumin is a fundamental regulator of the passage of liquids between compartments according to the current model.
As a drug it is obtained from human plasma and is used in solution at different concentrations for clinical use, being widely used in medicine and in the environment of the patient undergoing cardiac surgery as fluid therapy for its plasma-expanding properties with maintenance of oncotic pressure , antioxidant effect and as a transporter of molecules such as hormones, iron, bilirubin, free fatty acids, drugs and other elements, having a wide spectrum of indications. Unlike other colloids such as hydroxyethyl starch, its use has been associated with few negative effects.
Its use for priming the circuit of extracorporeal circulation during cardiac surgery has been commonly used, first of all for the ability to form a layer on the surface of the circuit, protecting blood from direct contact with its surface. It can cause protein denaturation, activation of the complement cascade, release of inflammatory mediators, and platelet activation. Secondly, the use of albumin in circuit priming can attenuate the drop in oncotic pressure due to a dilutional effect during the ECC period, an effect that can cause edema in the different organs with consequent dysfunction.
In a meta-analysis of the use of albumin in the priming of the CEC carried out in 2004, it was concluded that the priming with albumin preserved the platelet count better than the priming of the CEC with crystalloids, conserved the oncotic pressure better, favorably influenced fluid balance (less fluid requirement

Evidence for comparator:

Given the growing evidence that the use of albumin can decrease the incidence of acute kidney injury in patients with hypoalbuminemia who underwent cardiac surgery without ECC, that the majority of patients present hypoalbuminemia after ECC, together with the fact that the high incidence of ARD during the immediate postoperative period and to the widely studied properties of albumin, our interest is to investigate the use of albumin for patients undergoing cardiac surgery with ECC, using it for purging the circuit, since this period supposes, as described above,
a kidney injury perfectly delimited in time and clearly associated with a significant incidence of acute kidney injury, due to injury mechanisms that could be partially cushioned by the use of albumin, as a consequence of its properties.
This study aims to obtain information about the effect that albumin can have in this population of patients with a high incidence of acute kidney dysfunction, and if this benefit exists, to know whether or not it is significant to justify its systematic use.
Among the reasons that make this project potentially relevant from a scientific point of view, there is mainly the paucity of studies of this type that may allow establishing the recommendation for the use of albumin to reduce the incidence of ACC-DRA. Therefore, a great scientific impact of the results is expected.
From the health point of view, the results can have a high socio-economic impact, since the costs associated with the management of ARD are high, so an improvement in the cost-effectiveness ratio through the use of albumin can produce significant savings in the SNS.
We consider that this project will constitute a tool that will provide quality evidence, and its results could not only be the reason for publication in scientific journals, but also be included in clinical practice guidelines as a recommendation that allows optimizing the prognosis of patients who require undergoing cardiac surgery with ECC.

Actual start date of recruitment	02 November 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 248
Worldwide total number of subjects	248
EEA total number of subjects	248

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)	91
From 65 to 84 years	152
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

The population consists of patients who underwent cardiac surgery scheduled under ECC. Recruitment will take place at the pre-anesthetic visit.

Pre-assignment

Screening details:

Inclusion criteria: Adult patients (> 18 years) scheduled for cardiac surgery by ECC, who present GFR greater than or equal to 60 and left ventricular ejection fraction greater than or equal to 40%.
Exclu

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Blinding will not be necessary since the primed preparation of the CEC circuit will be performed by the infusion nursing team, and the solution with the experimental drug (albumin) looks the same as the solution without it.

Arms

Are arms mutually exclusive?	Yes
Arm title	Plasmalyte

Arm description:

Control treatment: Plasmalyte serum used for priming the extracorporeal circulation circuit.

Arm type	Active comparator
Investigational medicinal product name	Plasmalyte
Investigational medicinal product code	B05BB01
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Extracorporeal use

Dosage and administration details:

used during purged of CEC

Arm title	Albumin

Arm description:

Experimental treatment : Human Albumin for the priming of the CEC circuit , added to the usual solution (plasma serum) in sufficient quantity to achieve a concentration of 4% of the total priming volume versus usual priming with serum . plasmalyte .
Human albumin is already currently used for priming the CEC on certain occasions and in hospital centers.

Arm type	Active comparator
Investigational medicinal product name	Albumin
Investigational medicinal product code	B05A1
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Extracorporeal use

Dosage and administration details:

Albumin 4% used during purged of CEC

Number of subjects in period 1	Plasmalyte	Albumin
Started	122	126
Completed	122	126

Baseline characteristics

Reporting groups	
Reporting group title	Plasmalyte
Reporting group description:	
Control treatment: Plasmalyte serum used for priming the extracorporeal circulation circuit.	
Reporting group title	Albumin
Reporting group description:	
Experimental treatment : Human Albumin for the priming of the CEC circuit , added to the usual solution (plasma serum) in sufficient quantity to achieve a concentration of 4% of the total priming volume versus usual priming with serum . plasmalyte . Human albumin is already currently used for priming the CEC on certain occasions and in hospital centers.	

Reporting group values	Plasmalyte	Albumin	Total
Number of subjects	122	126	248
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)	45	46	91
From 65-84 years	75	77	152
85 years and over	2	3	5
Age continuous Units: years			
geometric mean	65.836	67.71	
standard deviation	± 12.9826	± 12.76	-
Gender categorical Units: Subjects			
Female	79	83	162
Male	43	43	86
Creatinine Units: micromole(s)/litre			
geometric mean	78.42	81.76	
standard deviation	± 11.89	± 14.20	-
GFR Units: mL/min/1.73m2			
geometric mean	80.48	76.09	
standard deviation	± 16.21	± 16.13	-
Albumin Units: gram(s)/litre			
geometric mean	40.774	41.083	
standard deviation	± 4.3416	± 3.5112	-

End points

End points reporting groups

Reporting group title	Plasmalyte
Reporting group description:	
Control treatment: Plasmalyte serum used for priming the extracorporeal circulation circuit.	
Reporting group title	Albumin
Reporting group description:	
Experimental treatment : Human Albumin for the priming of the CEC circuit , added to the usual solution (plasma serum) in sufficient quantity to achieve a concentration of 4% of the total priming volume versus usual priming with serum . plasmalyte . Human albumin is already currently used for priming the CEC on certain occasions and in hospital centers.	

Primary: AKI

End point title	AKI
End point description:	
End point type	Primary
End point timeframe:	
5 days	

End point values	Plasmalyte	Albumin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	126		
Units: Percentage				
AKI	38	37		
non AKI	84	89		

Statistical analyses

Statistical analysis title	Comparation
Comparison groups	Plasmalyte v Albumin
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≥ 0.05
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1 year

Adverse event reporting additional description:

All adverse events that occur will be collected and their causal relationship with the treatment received, severity and condition of unexpected will be evaluated.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Plasmalyte

Reporting group description:

Barcelona is not routinely applied to purge the CEC, it is carried out with crystalloid solution (plasmalyte serum), using albumin in CEC in certain exceptional circumstances (severe hypoproteinemia associated with anasarca, etc.) Control treatment: Plasmalyte serum used for priming the extracorporeal circulation circuit.

Reporting group title	Albumin

Reporting group description:

Experimental treatment : Human Albumin for the priming of the CEC circuit , added to the usual solution (plasma serum) in sufficient quantity to achieve a concentration of 4% of the total priming volume versus usual priming with serum . plasmalyte .
Human albumin is already currently used for priming the CEC on certain occasions and in hospital centers.

Serious adverse events	Plasmalyte	Albumin	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 122 (2.46%)	2 / 126 (1.59%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	0	2	
Blood and lymphatic system disorders			
Death	Additional description: Massive bleeding		
subjects affected / exposed	3 / 122 (2.46%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 2	

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

Non-serious adverse events	Plasmalyte	Albumin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 122 (11.48%)	14 / 126 (11.11%)	
Vascular disorders			
Shock			
subjects affected / exposed	9 / 122 (7.38%)	8 / 126 (6.35%)	
occurrences (all)	9	8	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	5 / 122 (4.10%)	5 / 126 (3.97%)	
occurrences (all)	5	5	
Blood and lymphatic system disorders			
Bleeding time normal			
subjects affected / exposed	0 / 122 (0.00%)	1 / 126 (0.79%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported