Clinical trial results:
Crystalloids or colloids for goal-directed fluid therapy with closed-loop assistance in major surgery?

Summary

EudraCT number	2014-005337-31
Trial protocol	BE
Global end of trial date	21 December 2017

Results information

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

Trial information

Trial identification

Sponsor protocol code	CHUB-fluides

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02312999
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU Brugmann
Sponsor organisation address	4 Place A. Van Gehuchten , Brussels, Belgium, 1020
Public contact	Service of Anesthesiology, CHU Brugmann, 32 024772330, Philippe.Vanderlinden@chu-brugmann.be
Scientific contact	Service of Anesthesiology, CHU Brugmann, 32 024772330 , Philippe.Vanderlinden@chu-brugmann.be

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	21 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 July 2017
Global end of trial reached?	Yes
Global end of trial date	21 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will examine whether there is a significant difference in postoperative outcomes between GDFT using a colloid solution versus a crystalloid solution.

Protection of trial subjects:

This clinical trial compares two intravenous solutions, with a marketing authorization, that are given according to the standard of care. Therefore, no additonal measures were taken apart from a monitoring of side effects, that were treated according to protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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	Belgium: 160
Worldwide total number of subjects	160
EEA total number of subjects	160

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)	81
From 65 to 84 years	79
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a monocentric trial in Belgium. Recruitment occured between April 2015 and November 2016.

Pre-assignment

Screening details:

Screening occured during the pre-anesthesia consultation. 198 patients were assessed for eligibility. 38 were excluded for the following reasons (4: atrial fibrillation, 7: preoperative renal failure, 1: aortic insufficiency, 7: decline to participate, 1: dementia, 4: logistic reasons, 1: jeovah witness, 1: minor patient, 12: hepatic disfunction).

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:

The randomization of the study (1:1) was created by the hospital pharmacist in blocks of 10. The morning of the surgey, blinded fluid solutions (visually identical plastic bags of 500ml) were delivered to the anesthesiologist in charge of the patient. The preparation, storage and dispensing of the study fluids was done independently by the hospital pharmacy of each institution. Study fluids were only identified by the assigned patient number.

Arms

Are arms mutually exclusive?	Yes
Arm title	Plasmalyte

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Plasmalyte
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 litres per day by intravenous use

Arm title	Volulyte

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Volulyte
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

33 mililiters/kg in total, intravenous use.

Number of subjects in period 1	Plasmalyte	Volulyte
Started	80	80
Completed	80	80

Baseline characteristics

Reporting groups	
Reporting group title	Plasmalyte
Reporting group description: -	
Reporting group title	Volulyte
Reporting group description: -	

Reporting group values	Plasmalyte	Volulyte	Total
Number of subjects	80	80	160
Age categorical			
Age			
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)	42	39	81
From 65-84 years	36	39	75
85 years and over	2	2	4
Age continuous			
Units: years			
median	62	65	
inter-quartile range (Q1-Q3)	48 to 70	53 to 73	-
Gender categorical			
Units: Subjects			
Female	29	35	64
Male	51	45	96

End points

End points reporting groups	
Reporting group title	Plasmalyte
Reporting group description: -	
Reporting group title	Volulyte
Reporting group description: -	

Primary: POMS score	
End point title	POMS score
End point description:	
Difference between the 2 groups in postoperative morbidity identified with the post-operative morbidity survey (POMS score) on postoperative day 2.	
End point type	Primary
End point timeframe:	
Postoperative day 2	

End point values	Plasmalyte	Volulyte		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: none	3	2		

Statistical analyses

Statistical analysis title	Chi square
Comparison groups	Plasmalyte v Volulyte
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the entire clinical trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	Clinical practice
Dictionary version	0
Reporting groups	
Reporting group title	Plasmalyte
Reporting group description: -	
Reporting group title	Volulyte
Reporting group description: -	

Serious adverse events	Plasmalyte	Volulyte	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 80 (22.50%)	15 / 80 (18.75%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Reoperation			
subjects affected / exposed	6 / 80 (7.50%)	3 / 80 (3.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Stroke			

subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Sepsis			
subjects affected / exposed	5 / 80 (6.25%)	3 / 80 (3.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bleeding requiring a redo surgery			
subjects affected / exposed	4 / 80 (5.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Anastomotic leak			
subjects affected / exposed	4 / 80 (5.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis			
subjects affected / exposed	4 / 80 (5.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	3 / 80 (3.75%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	5 / 80 (6.25%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 80 (3.75%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
Wound dehiscence			
subjects affected / exposed	4 / 80 (5.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal replacement therapy			
subjects affected / exposed	1 / 80 (1.25%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	18 / 80 (22.50%)	15 / 80 (18.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Plasmalyte	Volulyte	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 80 (62.50%)	35 / 80 (43.75%)	
Nervous system disorders			
Postoperative confusion			
subjects affected / exposed	4 / 80 (5.00%)	2 / 80 (2.50%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Paralytic ileus			
subjects affected / exposed	11 / 80 (13.75%)	7 / 80 (8.75%)	
occurrences (all)	1	1	
Postoperative nausea and vomiting			
subjects affected / exposed	26 / 80 (32.50%)	22 / 80 (27.50%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 80 (6.25%)	5 / 80 (6.25%)	
occurrences (all)	1	1	
Renal and urinary disorders			

Need for loop diuretics			
subjects affected / exposed	9 / 80 (11.25%)	4 / 80 (5.00%)	
occurrences (all)	1	1	
Infections and infestations			
Superficial wound infection			
subjects affected / exposed	5 / 80 (6.25%)	4 / 80 (5.00%)	
occurrences (all)	1	1	
Urinary and other infection			
subjects affected / exposed	21 / 80 (26.25%)	13 / 80 (16.25%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2015	- Increase of total trial duration - Modification of the end of trial definition - Addition of a long-term monitoring (6 months and 1 year after surgery) of the effects of the two fluids on renal and hepatic function, occurrence of pruritus, and quality of life.
24 August 2016	Increase of total amount of patients recruited.

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/30418217

http://www.ncbi.nlm.nih.gov/pubmed/29068831