Clinical trial results:
GDT in Urgent Abdominal Surgery - A Clinical Randomized Trial

Summary

EudraCT number	2015-000563-14
Trial protocol	DK
Global end of trial date	05 November 2018

Results information

Result version number	v1 (current)
This version publication date	23 May 2020
First version publication date	23 May 2020

Trial information

Trial identification

Sponsor protocol code	2014-734

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Holbaek Sygehus, Department of Surgery
Sponsor organisation address	Smedelundsgade 60, Holbaek, Denmark, 4300
Public contact	Surgical department, att. GAS-ART, Holbaek Sygehus, Research unit, +45 594840004344, bbrn@regionsjaelland.dk
Scientific contact	Surgical department, att. GAS-ART, Holbaek Sygehus, Research unit, +45 594840004344, bbrn@regionsjaelland.dk

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	04 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 November 2018
Global end of trial reached?	Yes
Global end of trial date	05 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We hypothesized that IV-fluid therapy to near maximum stroke volume followed by zero fluid balance could improve the outcome of patients undergoing major emergency surgery compared to IV-fluid therapy guided by blood pressure.

Protection of trial subjects:

Treated in routine care.

Background therapy:

Standard surgical and medical care of obstructive bowel disease or gastrointestinal perforation.

Evidence for comparator:

Best known standard of peroperative fluid care in patients undergoing emergency surgery for bowel obstruction or gastrointestinal perforation (according to PULP-trial and River´s study in patients with sepsis).

Actual start date of recruitment	01 August 2015
Long term follow-up planned	Yes
Long term follow-up rationale	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	Denmark: 304
Worldwide total number of subjects	304
EEA total number of subjects	304

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)	113
From 65 to 84 years	151
85 years and over	40

Subject disposition

Recruitment

Recruitment details:

Recruitment from 5 centres. August 2015 to august 2018.

Pre-assignment

Screening details:

We screened patients with radiologically verified obstructive bowel disease or gastrointestinal perforation.
Exclusion criteria was ASA 5, intraabdominal surgery within the last 30 days, dialysis on a regular basis, patients unable to give informed consent, children, pregnant women.

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Assessor blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	Flow controlled group

Arm description:

Fluid therapy controlled by stroke volume.

Arm type	Experimental
Investigational medicinal product name	Saline solution
Investigational medicinal product code	PR2
Other name	Sodium chloride solution 0.9%
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per day up to 4000 ml (adjusted individually) administered intravenously

Investigational medicinal product name	Human Albumin 5%
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per day up to 4000 ml (adjusted individually) administered intravenously.

Investigational medicinal product name	Ringer's solution
Investigational medicinal product code	PR3
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per day up to 4000 ml (adjusted individually) administered intravenously

Arm title	Pressure controlled group

Arm description:

Standard fluid therapy

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Flow controlled group	Pressure controlled group
Started	151	153
Completed	151	153

Baseline characteristics

Reporting groups	
Reporting group title	Flow controlled group
Reporting group description:	
Fluid therapy controlled by stroke volume.	
Reporting group title	Pressure controlled group
Reporting group description:	
Standard fluid therapy	

Reporting group values	Flow controlled group	Pressure controlled group	Total
Number of subjects	151	153	304
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)	50	63	113
From 65-84 years	79	72	151
85 years and over	22	18	40
Age continuous Units: years			
median	71	70	
inter-quartile range (Q1-Q3)	61 to 81	61 to 80	-
Gender categorical Units: Subjects			
Female	81	87	168
Male	70	66	136
Diagnosis Units: Subjects			
Obstructive bowel disease	116	115	231
Gastrointestinal perforation	35	38	73

End points

End points reporting groups

Reporting group title	Flow controlled group
Reporting group description:	
Fluid therapy controlled by stroke volume.	
Reporting group title	Pressure controlled group
Reporting group description:	
Standard fluid therapy	

Primary: Primary end point

End point title	Primary end point
End point description:	
Major complications defined by Clavien-Dindo grade IIIb to grade V.	
End point type	Primary
End point timeframe:	
Follow up 30 days and 90 days.	

End point values	Flow controlled group	Pressure controlled group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	153		
Units: 19	61	47		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Pressure controlled group v Flow controlled group
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Log hazard ratio

Secondary: Secondary end points

End point title	Secondary end points
End point description:	
Clavien-Dindo grade I to grade IIIa. Length of stay, time with mechanical respiratory support, time on dialysis, time in the intensive care unit.	

End point type	Secondary

End point timeframe:

From time of surgery and until 30 days postoperative.

End point values	Flow controlled group	Pressure controlled group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	153		
Units: 13	56	63		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Peri- and postoperative until hospital discharge.

Adverse event reporting additional description:

Event suspected directly related to the infusion of saline, albumin or Ringer's solution: acute anaphylactic reaction, hypernatremia (s-Na>155mmol/L), central pontine myelinolysis or seizures.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Flow

Reporting group description:

GDT

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: Not relevant

Serious adverse events	Flow		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 151 (0.66%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	0		
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	1 / 151 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Flow		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 151 (0.00%)		

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