Clinical trial results:
Perioperative Goal Directed Fluid Therapy during Esophageal Resection. A prospective randomized controlled open multi-centre trial to study the effect on postoperative complications

Summary

EudraCT number	2011-000254-39
Trial protocol	SE
Global end of trial date	30 April 2017

Results information

Result version number	v1 (current)
This version publication date	30 April 2024
First version publication date	30 April 2024

Trial information

Trial identification

Sponsor protocol code	2011-07-01 korr 121213

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01416077
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Region Östergötland
Sponsor organisation address	Universitetssjuhuset, Linköping, Sweden, 58183
Public contact	Lena Nilsson, Department of Anesthesia and Intensive Care, 46 0101031838, lena.nilsson@regionostergotland.se
Scientific contact	Lena Nilsson, Department of Anesthesia and Intensive Care, 46 0101031838, lena.nilsson@regionostergotland.se

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	30 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2015
Global end of trial reached?	Yes
Global end of trial date	30 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test whether intraoperative fluid and catecholamin administration steered by stroke volume optimization measured by "pulse contour analysis" will result in fewer postoperative complications

Protection of trial subjects:

Study approved by Ethics committee. Study participants protected from Swedish law.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 59
Worldwide total number of subjects	59
EEA total number of subjects	59

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)	23
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

After oral and written informed consent had been obtained adult patients scheduled for elective transthoracic oesophageal resection because of malignancy at University Hospital Linkoping or University Hospital Orebro were randomised.

Pre-assignment

Screening details:

Adult patients scheduled for elective transthoracic oesophageal resection because of malignancy were randomised.
Exclusion criteria were emergency procedures, planned colonic interposition, ASA class 4 or 5 patients or those for whom more extensive cardiac monitoring was planned, significant aortic or mitral valve insuffiency

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Goal-directed fluid therapy guided by pulse contour analysis

Arm type	Experimental
Investigational medicinal product name	dobutamine
Investigational medicinal product code	C01CA07
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initially 2,5µg/kg/min with the purpose to achieve cardiac index > 2,5 l/min/m2. Restrited by signs of cardiac ischemia or heart rate over 90 beats/min

Investigational medicinal product name	Volulyte
Investigational medicinal product code	23245
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

3 ml/kg (max 250 ml) as a bolus during 5 minutes. Wait for 5 minutes and evaluate change in heart stroke volume. If increased by more than 10%, repeat another bolus until no further increase over 10% in stroke volume or DO2i over 600 ml/min/m2.

Arm title	Control group

Arm description:

the responsible anaesthetist deter- mined the fluid administration rate and use of vasocon- strictors and inotropes. Stroke volume and Cardiac Index were not measured.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Intervention	Control group
Started	30	29
Completed	30	29

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Goal-directed fluid therapy guided by pulse contour analysis	
Reporting group title	Control group
Reporting group description:	
the responsible anaesthetist deter- mined the fluid administration rate and use of vasocon- strictors and inotropes. Stroke volume and Cardiac Index were not measured.	

Reporting group values	Intervention	Control group	Total
Number of subjects	30	29	59
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	65	66	
standard deviation	± 7	± 10	-
Gender categorical			
Units: Subjects			
Female	6	8	14
Male	24	21	45

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description:	
Goal-directed fluid therapy guided by pulse contour analysis	
Reporting group title	Control group
Reporting group description:	
the responsible anaesthetist deter- mined the fluid administration rate and use of vasocon- strictors and inotropes. Stroke volume and Cardiac Index were not measured.	

Primary: Postop complication after 5 days

End point title	Postop complication after 5 days
End point description:	
Postoperative days 0 to 5	
End point type	Primary
End point timeframe:	
Days	

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: number	56	33		

Statistical analyses

Statistical analysis title	postop compl 5 days
Comparison groups	Intervention v Control group
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Chi-squared

Primary: Postop complication after 30 days

End point title	Postop complication after 30 days
End point description:	
Accumulated number of complication after surgery up to 30 days postoperatively	
End point type	Primary

End point timeframe:
Postop 0 to 30 days

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of complications	124	81		

Statistical analyses

Statistical analysis title	Postop compl 30 days
Comparison groups	Intervention v Control group
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
o-30 days postoperatively	
Assessment type	Systematic

Dictionary used	
Dictionary name	Prespecified list of
Dictionary version	korr 12121

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Goal-directed fluid therapy guided by pulse contour analysis	
Reporting group title	Control group
Reporting group description:	
the responsible anaesthetist deter- mined the fluid administration rate and use of vasocon- strictors and inotropes. Stroke volume and Cardiac Index were not measured.	

Serious adverse events	Intervention	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 30 (73.33%)	19 / 29 (65.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	5 / 30 (16.67%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
unconsciosness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Obstruction			
subjects affected / exposed	6 / 30 (20.00%)	9 / 29 (31.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	14 / 30 (46.67%)	7 / 29 (24.14%)	
occurrences causally related to treatment / all	0 / 14	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	21 / 30 (70.00%)	12 / 29 (41.38%)	
occurrences causally related to treatment / all	0 / 21	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal injury			
subjects affected / exposed	1 / 30 (3.33%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory insuffiency			
subjects affected / exposed	7 / 30 (23.33%)	5 / 29 (17.24%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Seroma			
subjects affected / exposed	1 / 30 (3.33%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 30 (13.33%)	2 / 29 (6.90%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Intervention	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 30 (86.67%)	22 / 29 (75.86%)	
Cardiac disorders			
Pericardial fluid			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	10 / 30 (33.33%)	7 / 29 (24.14%)	
occurrences (all)	10	7	
Surgical and medical procedures			
Pain			
subjects affected / exposed	1 / 30 (3.33%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Nervous system disorders			
Delirium			
subjects affected / exposed	6 / 30 (20.00%)	0 / 29 (0.00%)	
occurrences (all)	6	0	
Blood and lymphatic system disorders			
Coagulation factor			
subjects affected / exposed	7 / 30 (23.33%)	5 / 29 (17.24%)	
occurrences (all)	7	5	
Gastrointestinal disorders			
Paralytic ileus			
subjects affected / exposed	6 / 30 (20.00%)	3 / 29 (10.34%)	
occurrences (all)	6	3	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	11 / 30 (36.67%)	5 / 29 (17.24%)	
occurrences (all)	11	5	
Renal and urinary disorders			
Transient renal impairment			
subjects affected / exposed	4 / 30 (13.33%)	2 / 29 (6.90%)	
occurrences (all)	4	2	
Infections and infestations			
Pneumonia or other minor infections			
subjects affected / exposed	19 / 30 (63.33%)	15 / 29 (51.72%)	
occurrences (all)	19	15	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30431499