Clinical trial results:
Effect of sevoflurane and propofol on hepato-splanchnic pressure and flow during hepatobiliary surgery.

Summary

EudraCT number	2017-000071-90
Trial protocol	BE
Global end of trial date	27 January 2018

Results information

Result version number	v1 (current)
This version publication date	01 May 2020
First version publication date	01 May 2020

Trial information

Trial identification

Sponsor protocol code	AGO/2017/002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03772106
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ghent University Hospital
Sponsor organisation address	C. Heymanslaan 10, Ghent, Belgium,
Public contact	Bimetra Clinics, Ghent University Hospital, Bimetra.Clinics@uzgent.be
Scientific contact	Bimetra Clinics, Ghent University Hospital, Bimetra.Clinics@uzgent.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	10 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2018
Global end of trial reached?	Yes
Global end of trial date	27 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of the study is to compare the effect of sevoflurane and propofol on hepato-splanchnic pressure and blood flow during hepatobiliary surgery. We hypothesized that sevoflurane induces a dose-dependent reduction of hepato-splanchnic blood flow, while propofol increases hepato-splanchnic blood flow.

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 June 2017
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	8
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

35 patients were screened in the period from 08-Jun-2017 till 27-Jan-2017. 29 patients were included, 27 patients were randomised. 18 patients were included and completed the trial. End of trial notification was dated 27-Jan-2018 (last patient last visit) and submitted to EC and CA 16-Nov-2108.

Pre-assignment

Screening details:

Inclusion Criteria
- adult >+ 18 years (Female or Male)
- ASA I-II-III
-able to comprehend, sign and date the written consent document to participate in the clinical trial
- sheduled for hepato-biliary surgery

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	group S

Arm description:

Sevoflurane

Arm type	Experimental
Investigational medicinal product name	Sevoflurane
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Sevoflurane will be titrated according to BIS value between 45-55, which is an adequate depth of anesthesia for surgery

Arm title	group P

Arm description:

propofol 1%

Arm type	Experimental
Investigational medicinal product name	propofol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Propofol will be titrated according to a Bispectral Index (BIS) value between 45-55, which is an adequate depth of anesthesia for surgery

Number of subjects in period 1	group S	group P
Started	9	9
Completed	9	9

Baseline characteristics

Reporting groups	
Reporting group title	group S
Reporting group description: Sevoflurane	
Reporting group title	group P
Reporting group description: propofol 1%	

Reporting group values	group S	group P	Total
Number of subjects	9	9	18
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)	4	4	8
From 65-84 years	5	5	10
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	63.9	63.6	
standard deviation	± 12	± 5.4	-
Gender categorical Units: Subjects			
Female	3	4	7
Male	6	5	11
smoker Units: Subjects			
smoker	5	1	6
non-smoker	4	8	12
ASA (American Society of Anaestesiologist physical status) Units: Subjects			
ASA I	0	1	1
ASA II	6	3	9
ASA III	3	5	8
Somatostatin			
Patients received somatostatin at 250 g h-1 to reduce pancreatic secretion.			
Units: Subjects			
yes	5	4	9
no	4	5	9

BMI Units: kg/m² arithmetic mean standard deviation	 23.3 ± 2.5	 25.2 ± 2.5	 -
length Units: cm arithmetic mean standard deviation	 169.8 ± 7.9	 169.1 ± 8.8	 -
Systolic Blood Pressure Units: mmHg arithmetic mean standard deviation	 125 ± 16	 133 ± 12	 -
Diastolic Blood Pressure Units: mmHg arithmetic mean standard deviation	 76 ± 11	 78 ± 7	 -
Heart Rate Units: bpm arithmetic mean standard deviation	 73 ± 10	 72 ± 2	 -
weight Units: kg arithmetic mean standard deviation	 67.4 ± 9.9	 72.0 ± 7.5	 -

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mmHg				
arithmetic mean (standard deviation)				
T1	8.7 (± 2.7)	10.1 (± 6.0)		
T2	9.9 (± 4.4)	6.0 (± 3.1)		
T3	8.6 (± 5.2)	8.3 (± 4.2)		

Statistical analyses

No statistical analyses for this end point

Primary: P. Cava

End point title	P. Cava[3]

End point description:

End point type	Primary

End point timeframe:

P. Cava measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mmHg				
arithmetic mean (standard deviation)				
T1	5.4 (± 3.2)	6.4 (± 2.9)		
T2	6.7 (± 3.9)	5.4 (± 2.6)		
T3	7.2 (± 2.6)	6.7 (± 4.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Pulsatility Index (PI PV)

End point title	Pulsatility Index (PI PV)[4]

End point description:

End point type	Primary

End point timeframe:

PI PV measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non-applicable				
arithmetic mean (standard deviation)				
T1	0.5 (± 0.3)	0.4 (± 0.2)		
T2	0.5 (± 0.3)	0.3 (± 0.2)		
T3	0.5 (± 0.2)	0.5 (± 0.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Pulsatility Index (PI HA)

End point title	Pulsatility Index (PI HA)[5]

End point description:

End point type	Primary

End point timeframe:

PI HA measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non-aplicable				
arithmetic mean (standard deviation)				
T1	1.7 (± 0.9)	1.4 (± 0.9)		
T2	1.5 (± 0.7)	1.4 (± 0.6)		
T3	1.5 (± 0.5)	1.4 (± 0.7)		

Statistical analyses

No statistical analyses for this end point

Primary: total HBF

End point title	total HBF[6]

End point description:

End point type	Primary

End point timeframe:

Total HBF measured at baseline (T1), post-resection (T2) and pre-reconstruction (T3)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: ml/min				
arithmetic mean (standard deviation)				
t1	1003 (± 411)	997 (± 344)		
T2	860 (± 318)	937 (± 231)		
T3	943 (± 225)	998 (± 264)		

Statistical analyses

No statistical analyses for this end point

Primary: PVF

End point title	PVF[7]

End point description:

End point type	Primary

End point timeframe:

PVF measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: ml/min				
arithmetic mean (standard deviation)				
T1	790 (± 317)	760 (± 275)		
T2	612 (± 218)	687 (± 203)		
T3	704 (± 137)	714 (± 210)		

Statistical analyses

No statistical analyses for this end point

Primary: HAF

End point title	HAF[8]

End point description:

End point type	Primary

End point timeframe:

HAF measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: ml/min				
arithmetic mean (standard deviation)				
T1	212 (± 138)	237 (± 150)		
T2	247 (± 199)	249 (± 110)		
T3	239 (± 149)	284 (± 101)		

Statistical analyses

No statistical analyses for this end point

Primary: Rel. HAF

End point title	Rel. HAF[9]

End point description:

End point type	Primary

End point timeframe:

Rel. HAF measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: percentage				
arithmetic mean (standard deviation)				
T1	4.1 (± 3.4)	4.8 (± 2.8)		
T2	4.4 (± 3.7)	4.6 (± 1.9)		
T3	4.6 (± 3.5)	5.3 (± 2.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Rel. PVF

End point title	Rel. PVF[10]

End point description:

End point type	Primary

End point timeframe:

Rel. PVF measured at baseline (T1), post resection (T2) and pre reconstruction (T3)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: no statistical analysis available

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: percentage				
arithmetic mean (standard deviation)				
T1	15.9 (± 9.4)	15.2 (± 5.2)		
T2	11.1 (± 5.3)	12.8 (± 3.7)		
T3	12.8 (± 3.8)	13.1 (± 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Arterial Pressure (MAP)

End point title	Mean Arterial Pressure (MAP)

End point description:

End point type	Secondary

End point timeframe:

MAP measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mmHg				
arithmetic mean (standard deviation)				
T0	80 (± 11.3)	80 (± 8.7)		
T1	69 (± 10.2)	82 (± 9.5)		
T2	74 (± 8.6)	76 (± 5.3)		
T3	76 (± 8.6)	82 (± 4.5)		
T4	70 (± 7.6)	75 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate (HR)

End point title	Heart Rate (HR)

End point description:

End point type	Secondary

End point timeframe:

HR measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: bpm				
arithmetic mean (standard deviation)				
T0	60 (± 9.1)	60 (± 9.6)		
T1	78 (± 14.0)	75 (± 12.5)		
T2	80 (± 10.9)	79 (± 9.9)		
T3	79 (± 12.3)	77 (± 8.3)		
T4	79 (± 10.1)	76 (± 9.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Central Venous Pressure (CVP)

End point title	Central Venous Pressure (CVP)

End point description:

End point type	Secondary

End point timeframe:

CVP measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mmHg				
arithmetic mean (standard deviation)				
T0	10 (± 3)	7 (± 2)		
T1	5 (± 2)	5 (± 2)		
T2	5 (± 4)	5 (± 1)		
T3	6 (± 2)	4 (± 2)		
T4	6 (± 1)	5 (± 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cardiac Index (CI)

End point title	Cardiac Index (CI)

End point description:

End point type	Secondary

End point timeframe:

CI measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: l/(min.m²)				
arithmetic mean (standard deviation)				
T0	2.6 (± 0.5)	2.5 (± 0.3)		
T1	3.1 (± 0.8)	2.7 (± 0.4)		
T2	3.3 (± 0.6)	3.0 (± 0.5)		
T3	3.2 (± 0.6)	3.0 (± 0.4)		
T4	3.3 (± 0.9)	3.0 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pulse Pressure Variation (PPV)

End point title	Pulse Pressure Variation (PPV)

End point description:

End point type	Secondary

End point timeframe:

PPV measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: percentage				
arithmetic mean (standard deviation)				
T0	5 (± 2.9)	6 (± 2.3)		
T1	8 (± 4.6)	9 (± 4.0)		
T2	10 (± 5.6)	9 (± 1.7)		
T3	8 (± 5.8)	8 (± 3.0)		
T4	8 (± 5.2)	7 (± 2.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: lactate

End point title	lactate

End point description:

End point type	Secondary

End point timeframe:

lactate measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mg/dL				
arithmetic mean (standard deviation)				
T0	9.7 (± 1.8)	8.7 (± 1.7)		
T1	12.2 (± 3.8)	8.9 (± 1.5)		
T2	16.3 (± 6.8)	10.1 (± 2.7)		
T3	18.2 (± 8.4)	10.5 (± 2.9)		
T4	22.4 (± 8.4)	12.5 (± 5.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PaCO2

End point title	PaCO2

End point description:

End point type	Secondary

End point timeframe:

PaCO2 measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mmHg				
arithmetic mean (standard deviation)				
T0	41 (± 6.5)	40 (± 5.7)		
T1	42 (± 5.9)	42 (± 4.5)		
T2	43 (± 4.8)	41 (± 6.1)		
T3	42 (± 5.1)	42 (± 3.3)		
T4	40 (± 3.0)	40 (± 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: pH

End point title	pH

End point description:

End point type	Secondary

End point timeframe:

pH measured at baseline (T0 and T1), post resection (T2), pre reconstruction (T3) and end of surgery (T4)

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: non applicable				
arithmetic mean (standard deviation)				
T0	7.35 (± 0.07)	7.38 (± 0.05)		
T1	7.34 (± 0.05)	7.36 (± 0.05)		

T2	7.33 (± 0.05)	7.35 (± 0.05)		
T3	7.35 (± 0.06)	7.34 (± 0.04)		
T4	7.35 (± 0.06)	7.36 (± 0.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: amount of bloodloss

End point title	amount of bloodloss

End point description:

End point type	Secondary

End point timeframe:
from start of surgery until end of surgery

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: ml				
arithmetic mean (standard deviation)	689 (± 448)	567 (± 212)		

Statistical analyses

No statistical analyses for this end point

Secondary: amount of colloids given during surgery

End point title	amount of colloids given during surgery

End point description:

End point type	Secondary

End point timeframe:
from start of surgery until end of surgery

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: ml				
arithmetic mean (standard deviation)	1078 (± 441)	1067 (± 500)		

Statistical analyses

No statistical analyses for this end point

Secondary: need of ephedrine

End point title	need of ephedrine

End point description:

End point type	Secondary

End point timeframe:
from start of anesthesia until end of anesthesia

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mg				
arithmetic mean (standard deviation)	10.3 (± 5.6)	5.3 (± 3.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: need of phenylephrine

End point title	need of phenylephrine

End point description:

End point type	Secondary

End point timeframe:
from start anesthesia until end of anesthesia

End point values	group S	group P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mg				
arithmetic mean (standard deviation)	0.37 (± 0.4)	0.16 (± 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: need of noradrenaline

End point title	need of noradrenaline

End point description:

End point type	Secondary

End point timeframe:
from start of anesthesia until end of anesthesia

End point values	group S	group P		

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: overall study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0

Reporting groups	
Reporting group title	group S
Reporting group description: -	
Reporting group title	group P
Reporting group description: -	

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 events were recorded for the participating patients

Serious adverse events	group S	group P	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Hepatobiliary disorders			
Biliary anastomosis complication	Additional description: Bile duct leakage after surgery		
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	group S	group P	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported