Clinical trial results:
Anesthesia Induced Hormonal Oliguria Trial

Summary

EudraCT number	2017-001646-10
Trial protocol	SE
Global end of trial date	10 January 2020

Results information

Result version number	v1 (current)
This version publication date	07 April 2022
First version publication date	07 April 2022

Trial information

Trial identification

Sponsor protocol code	ANIMAL-523-2014-2569

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03336801
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Uppsala University
Sponsor organisation address	Dept surgical sciences, Uppsala university , Uppsala, Sweden, 75185
Public contact	Uppsala University Hospital, Uppsala University Hospital, 46 186119209, suzanne.odeberg.wernerman@akademiska.se
Scientific contact	Uppsala University Hospital, Uppsala University Hospital, 46 186119209, suzanne.odeberg.wernerman@akademiska.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	23 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2020
Global end of trial reached?	Yes
Global end of trial date	10 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate changes in renal function during general anaesthesia.

Protection of trial subjects:

Normal clinical procedures to reduce stress and pain.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 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	Sweden: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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

Subject disposition

Recruitment

Recruitment details:

Patients scheduled for elective spinal surgery were enrolled aug 2017 - jan 2020 at Uppsala University Hospital (Akademiska sjukhuset) in the preoperative ward.

Pre-assignment

Screening details:

Inclusion criteria: 18-65 years old, elective spinal surgery, signed consent.
Exclusion criteria: patient refusal, pregnancy/breast feeding, allergy to anesthesia, ASA class 3-5, NYHA class 3-4, BMI >37, insulin-treated diabetes, kidney disease, liver disease, genetic malignant hyperthermia.

Pre-assignment period milestones

Number of subjects started	36
Number of subjects completed	36

Period 1

Period 1 title	Pre-anesthesia
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Propofol

Arm description:

Anesthesia maintenance by propofol.

Arm type	Active comparator
Investigational medicinal product name	Diprivan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion of intravenous propofol (20 mg/ml) to maintain target controlled-infusion of 4-6 mikrog/ml.

Arm title	Sevoflurane

Arm description:

Anesthesia maintenence by sevoflurane.

Arm type	Active comparator
Investigational medicinal product name	Sevorane (Abbvie)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Sevoflurane was administered to maintain minimal alveolar concentration 0.8-1.2 at a fresh gas flow rate of 0.3-0.5 l/min.

Number of subjects in period 1	Propofol	Sevoflurane
Started	18	18
Completed	16	17
Not completed	2	1
Protocol deviation	2	1

Period 2

Period 2 title	During anesthesia (before surgery)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Propofol

Arm description:

Anesthesia maintenance by propofol.

Arm type	Active comparator
Investigational medicinal product name	Diprivan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion of intravenous propofol (20 mg/ml) to maintain target controlled-infusion of 4-6 mikrog/ml.

Arm title	Sevoflurane

Arm description:

Anesthesia maintenence by sevoflurane.

Arm type	Active comparator
Investigational medicinal product name	Sevorane (Abbvie)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Sevoflurane was administered to maintain minimal alveolar concentration 0.8-1.2 at a fresh gas flow rate of 0.3-0.5 l/min.

Number of subjects in period 2	Propofol	Sevoflurane
Started	16	17
Completed	13	14
Not completed	3	3
Consent withdrawn by subject	-	1
Protocol deviation	3	2

Period 3	
Period 3 title	During postoperative care
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms	
Are arms mutually exclusive?	Yes
Arm title	Propofol
Arm description: Anesthesia maintenance by propofol.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Sevoflurane
Arm description: Anesthesia maintenence by sevoflurane.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Propofol	Sevoflurane
Started	13	14
Finished 2h sampling period	13	14
Completed	13	14

Period 4	
Period 4 title	The day after (surgical ward)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms	
Are arms mutually exclusive?	Yes
Arm title	Propofol

Arm description:

Anesthesia maintenance by propofol.

Arm type	Active comparator
Investigational medicinal product name	Diprivan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion of intravenous propofol (20 mg/ml) to maintain target controlled-infusion of 4-6 mikrog/ml.

Arm title	Sevoflurane

Arm description:

Anesthesia maintenence by sevoflurane.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Propofol	Sevoflurane
Started	13	14
Finished 2h sampling period	13	14
Completed	13	14

Baseline characteristics

Reporting groups	
Reporting group title	Propofol
Reporting group description:	
Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description:	
Anesthesia maintenence by sevoflurane.	

Reporting group values	Propofol	Sevoflurane	Total
Number of subjects	18	18	36
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)	18	18	36
From 65-84 years	0	0	0
85 years and over	0	0	0
Not recorded	0	0	0
Age continuous Units: years			
median	48	53	
full range (min-max)	43 to 53	49 to 58	-
Gender categorical Units: Subjects			
Female	8	6	14
Male	10	12	22
AHA Units: Subjects			
Class 1	12	11	23
Class 2	6	7	13
ASA Units: Subjects			
Class 1	13	13	26
Class 2	5	5	10
BMI Units: N/A			
median	27	29	
full range (min-max)	18 to 34	18 to 36	-

End points

End points reporting groups

Reporting group title	Propofol
Reporting group description: Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description: Anesthesia maintenence by sevoflurane.	
Reporting group title	Propofol
Reporting group description: Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description: Anesthesia maintenence by sevoflurane.	
Reporting group title	Propofol
Reporting group description: Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description: Anesthesia maintenence by sevoflurane.	
Reporting group title	Propofol
Reporting group description: Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description: Anesthesia maintenence by sevoflurane.	

Primary: Urine output

End point title	Urine output
End point description:	
End point type	Primary
End point timeframe: Urine output was measured as of induction of anesthesia and measured the last time the day after surgery.	

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: ml/kg/h				
least squares mean (standard deviation)	1.1 (± 1.0)	0.3 (± 0.2)	1.8 (± 1.9)	1.3 (± 0.7)

End point values	Propofol	Sevoflurane		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: ml/kg/h				
least squares mean (standard deviation)	2.0 (± 1.0)	1.5 (± 1.1)		

Statistical analyses

Statistical analysis title	Urine output

Statistical analysis description:

2x3 repeated measurements ANOVA with Tukey's HSD

Comparison groups	Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane
Number of subjects included in analysis	81
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	ANOVA

Primary: Plasma creatinine

End point title	Plasma creatinine

End point description:

End point type	Primary

End point timeframe:

From pre-operative until the next day, 24h after surgery.

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	13	14
Units: microgram(s)/millilitre				
least squares mean (standard deviation)	67 (± 12)	76 (± 17)	63 (± 12)	74 (± 15)

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: microgram(s)/millilitre				
least squares mean (standard deviation)	68 (± 12)	81 (± 15)	62 (± 9)	71 (± 14)

Statistical analyses

Statistical analysis title	Plasma creatinine
Statistical analysis description: 2x4 repeated measurements ANOVA with Tukey's HSD	
Comparison groups	Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane
Number of subjects included in analysis	109
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	ANOVA

Secondary: Plasma renin

End point title	Plasma renin
End point description:	
End point type	Secondary
End point timeframe: From pre-operatively to the next day, 24h after surgery.	

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: mIU/L				
least squares mean (standard deviation)	12 (± 10)	23 (± 20)	27 (± 24)	138 (± 131)

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: mIU/L				
least squares mean (standard deviation)	26 (± 32)	82 (± 135)	14 (± 13)	27 (± 18)

Statistical analyses

Statistical analysis title	Plasma renin
Statistical analysis description:	
2x4 repeated measurement ANOVA with Bonferroni corrected planned comparisons	
Comparison groups	Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANOVA

Secondary: KIM-1	
End point title	KIM-1
End point description:	
End point type	Secondary
End point timeframe:	
From during anesthesia until the next day, 24h after surgery.	

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: picogram/milliliter				
least squares mean (standard deviation)	959 (± 855)	1070 (± 694)	659 (± 571)	1149 (± 733)

End point values	Propofol	Sevoflurane		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: picogram/milliliter				
least squares mean (standard deviation)	577 (± 373)	996 (± 383)		

Statistical analyses

Statistical analysis title	KIM-1
Statistical analysis description:	
2x3 repeated measurements ANOVA with Tukey's HSD	
Comparison groups	Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane

Number of subjects included in analysis	81
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	ANOVA

Secondary: Vasopressin

End point title	Vasopressin

End point description:

End point type	Secondary

End point timeframe:

From pre-operative to the next day, 24h after surgery.

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: picogram/milliliter				
least squares mean (standard deviation)	11 (± 7)	12 (± 7)	13 (± 7)	17 (± 14)

End point values	Propofol	Sevoflurane	Propofol	Sevoflurane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	14	13	14
Units: picogram/milliliter				
least squares mean (standard deviation)	15 (± 11)	27 (± 24)	15 (± 8)	29 (± 38)

Statistical analyses

Statistical analysis title	Vasopressin

Statistical analysis description:

2x4 repeated measurements ANOVA with Tukey's HSD

Comparison groups	Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane v Propofol v Sevoflurane
Number of subjects included in analysis	108
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	ANOVA

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From the first sampling (before surgery) until the last sampling (24 hours after surgery).	
Assessment type	Systematic

Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	211130

Reporting groups	
Reporting group title	Propofol
Reporting group description: Anesthesia maintenance by propofol.	
Reporting group title	Sevoflurane
Reporting group description: Anesthesia maintenence by sevoflurane.	

Serious adverse events	Propofol	Sevoflurane	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Propofol	Sevoflurane	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	

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 adverse events related to the trial were reported.

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? Yes

Date	Interruption	Restart date
10 January 2020	Covid-19 pandemic	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The clinical trial was terminated early due to logistical changes in the hospital because of the Covid-19 pandemic.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35279277