



## Clinical trial results:

### Intraoperative methadone in same-day hysterectomy: a prospective, double-blind, randomised controlled trial

#### Summary

EudraCT number	2018-004351-20
Trial protocol	DK
Global end of trial date	06 October 2022

#### Results information

Result version number	v1 (current)
This version publication date	01 October 2023
First version publication date	01 October 2023
Summary attachment (see zip file)	BMJ atricle (Clinical effectiveness and safety of intraoperative methadone in patients undergoing laparoscopic hysterectomy a randomised, blinded clinical trial.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	01122018v2
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03908060
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Lone Nikolajsen, Aarhus University Hospital, 0045 78464317, lone.nikolajsen@clin.au.dk
Scientific contact	Lone Nikolajsen, Aarhus University Hospital, 0045 78464317, lone.nikolajsen@clin.au.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	01 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2022
Global end of trial reached?	Yes
Global end of trial date	06 October 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The aim of this study is to investigate the effect of a single dose of intravenous intraoperative methadone on postoperative opioid consumption, pain and side effects in patients scheduled for hysterectomy for benign indications. A single dose of intravenous intraoperative morphine will be used as an active comparator.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and Guidelines for Good Clinical Practice (GCP) and monitored by the GCP unit at Aarhus University Hospital, Aarhus, Denmark. The study protocol was approved by the Danish Protection Agency (ID 1-16-02-747-18), the Central Denmark Region Committees on Health Research Ethics (ID 1-10-72-365-18), and the Danish Health and Medicines Authority (ID 2018-004351-20).

Background therapy:

Laparoscopic hysterectomy is often carried out as day-stay surgery. Minimising postoperative pain is therefore of utmost importance to ensure timely discharge from hospital. Methadone has several desirable pharmacological features, including a long elimination half-life. Therefore, a single intraoperative dose could provide long-lasting pain relief.

Evidence for comparator: -

Actual start date of recruitment	22 April 2019
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	Denmark: 163
Worldwide total number of subjects	163
EEA total number of subjects	163

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)	152
From 65 to 84 years	11
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were screened for inclusion at the first ambulatory contact at Horsens Regional Hospital, Horsens, Denmark, and informed oral and written consent was obtained before surgery. Adult females scheduled for day-stay, elective, laparoscopic hysterectomy were enrolled.

### Pre-assignment

Screening details:

Patients were screened for inclusion at the first ambulatory contact at Horsens Regional Hospital, Horsens, Denmark, and informed oral and written consent was obtained before surgery. Adult females scheduled for day-stay, elective, laparoscopic hysterectomy were enrolled.

### Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Intervention

Arm description:

A 10 mL syringe with 2 mg/mL of methadone was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

Arm type	Experimental
Investigational medicinal product name	Methadone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intravenous bolus use

Dosage and administration details:

A 10 mL syringe with 2 mg/mL of methadone was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

<b>Arm title</b>	Control
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Arm description:

A 10 mL syringe with 2 mg/mL of morphine was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

Arm type	Active comparator
Investigational medicinal product name	Morphine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intravenous bolus use

Dosage and administration details:

A 10 mL syringe with 2 mg/mL of morphine was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

<b>Number of subjects in period 1</b>	Intervention	Control
Started	81	82
Completed	64	63
Not completed	17	19
Consent withdrawn by subject	4	2
Inoperable	1	2
Converted to open surgery	2	3
Did not receive study drug from hospital pharmacy	6	8
Surgery postponed to after study completion	1	-
Prolonged QT interval	3	4

## Baseline characteristics

### Reporting groups

Reporting group title	Intervention
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Reporting group description:

A 10 mL syringe with 2 mg/mL of methadone was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

Reporting group title	Control
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Reporting group description:

A 10 mL syringe with 2 mg/mL of morphine was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.

Reporting group values	Intervention	Control	Total
Number of subjects	81	82	163
Age categorical Units: Subjects			
Adults (18-64 years)	76	76	152
From 65-84 years	5	6	11
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	81	82	163
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	Intervention
Reporting group description: A 10 mL syringe with 2 mg/mL of methadone was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.	
Reporting group title	Control
Reporting group description: A 10 mL syringe with 2 mg/mL of morphine was prepared. The dose of the study drug was be administered as intravenous bolus dose in equipotent doses (0.2 mg/kg) corresponding to 1 mL for every 10 kg of ideal body weight (height [cm]—105), rounded to the nearest half.	

### Primary: Opioid consumption 024 hours

End point title	Opioid consumption 024 hours
End point description:	
End point type	Primary
End point timeframe: Opioid consumption 024 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: mg				
median (inter-quartile range (Q1-Q3))	42 (10 to 67)	54.5 (31 to 83)		

### Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Intervention v Control
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

### Primary: Opioid consumption 06 hours

End point title	Opioid consumption 06 hours
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End point description:

End point type	Primary
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End point timeframe:

Opioid consumption 06 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: mg				
median (inter-quartile range (Q1-Q3))	35.5 (0 to 61)	48 (31 to 74.5)		

### Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Intervention v Control
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

### Secondary: Pain intensity (NRS, 010) at rest at 1 hour

End point title	Pain intensity (NRS, 010) at rest at 1 hour
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at rest at 1 hour

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 4)	3 (2 to 5)		

### Statistical analyses



No statistical analyses for this end point

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**Secondary: Pain intensity (NRS, 010) at rest at 6 hours**

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End point title	Pain intensity (NRS, 010) at rest at 6 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at rest at 6 hours

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End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	2 (1 to 3)		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Pain intensity (NRS, 010) at rest at 24 hours**

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End point title	Pain intensity (NRS, 010) at rest at 24 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at rest at 24 hours

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End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	2 (1 to 4)		

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Pain intensity (NRS, 010) at rest at 48 hours**

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End point title	Pain intensity (NRS, 010) at rest at 48 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at rest and at 48 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	3 (1 to 3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Patient satisfaction (NRS, 010) with pain management at 3 hours

End point title	Patient satisfaction (NRS, 010) with pain management at 3 hours
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End point description:

End point type	Secondary
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End point timeframe:

Patient satisfaction (NRS, 010) with pain management at 3 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	10 (9 to 10)	10 (9 to 10)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Patient satisfaction (NRS, 010) with pain management at 24 hours

End point title	Patient satisfaction (NRS, 010) with pain management at 24 hours
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End point description:

End point type	Secondary
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End point timeframe:

Patient satisfaction (NRS, 010) with pain management at 24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	9 (7 to 10)	9 (8 to 10)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: PONV (none/mild/moderate/severe) at 6 hours

End point title	PONV (none/mild/moderate/severe) at 6 hours
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End point description:

End point type	Secondary
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End point timeframe:

PONV (none/mild/moderate/severe) at 6 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
None or mild	49	42		
Moderate or severe	15	20		

### Statistical analyses

No statistical analyses for this end point

### Secondary: PONV (none/mild/moderate/severe) at 24 hours

End point title	PONV (none/mild/moderate/severe) at 24 hours
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End point description:

End point type	Secondary
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End point timeframe:

PONV (none/mild/moderate/severe) at 24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
None or mild	49	51		
Moderate or severe	15	12		

### Statistical analyses

No statistical analyses for this end point

### Secondary: PONV (none/mild/moderate/severe) at 72 hours

End point title	PONV (none/mild/moderate/severe) at 72 hours
End point description:	
End point type	Secondary
End point timeframe:	
PONV (none/mild/moderate/severe) at 72 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
None or mild	56	59		
Moderate or severe	7	4		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Ramsey Sedation Scale, Level 2, 0.5 hours

End point title	Ramsey Sedation Scale, Level 2, 0.5 hours
End point description:	
End point type	Secondary
End point timeframe:	
Ramsey Sedation Scale, Level 2, 0.5 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	50	47		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Ramsey Sedation Scale, Level 2, 1 hour

End point title	Ramsey Sedation Scale, Level 2, 1 hour
End point description:	
End point type	Secondary
End point timeframe:	
Ramsey Sedation Scale, Level 2, 1 hour	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	44	45		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Ramsey Sedation Scale, Level 2, 3 hours

End point title	Ramsey Sedation Scale, Level 2, 3 hours
End point description:	
End point type	Secondary
End point timeframe:	
Ramsey Sedation Scale, Level 2, 3 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	52	57		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Ventilatory frequency <10 min in PACU

End point title	Ventilatory frequency <10 min in PACU
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End point description:

End point type	Secondary
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End point timeframe:

In PACU

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	1	1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Oxygen saturation <94% in PACU

End point title	Oxygen saturation <94% in PACU
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End point description:

End point type	Secondary
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End point timeframe:

In PACU

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	0	1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain intensity (NRS, 010) at coughing at 1 hour

End point title	Pain intensity (NRS, 010) at coughing at 1 hour
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at coughing at 1 hour

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	4 (3 to 6)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain intensity (NRS, 010) at coughing at 6 hours

End point title	Pain intensity (NRS, 010) at coughing at 6 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at coughing at 6 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	3 (2 to 5)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain intensity (NRS, 010) at coughing at 24 hours

End point title	Pain intensity (NRS, 010) at coughing at 24 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at coughing at 24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	5 (3 to 7)	5 (3 to 7)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain intensity (NRS, 010) at coughing at 48 hours

End point title	Pain intensity (NRS, 010) at coughing at 48 hours
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End point description:

End point type	Secondary
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End point timeframe:

Pain intensity (NRS, 010) at coughing at 48 hours



End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	4 (3 to 6)	5 (3 to 7)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at rest at 0.5 hour

End point title	Pain intensity (NRS, 010) at rest at 0.5 hour
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at rest at 0.5 hour	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	5 (3 to 6)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at coughing at 0.5 hour

End point title	Pain intensity (NRS, 010) at coughing at 0.5 hour
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at coughing at 0.5 hour	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3.5 (3 to 6)	5 (4 to 7)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at rest at 3 hours

End point title	Pain intensity (NRS, 010) at rest at 3 hours
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at rest at 3 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	2 (1 to 3)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at coughing at 3 hours

End point title	Pain intensity (NRS, 010) at coughing at 3 hours
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at coughing at 3 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (2 to 4)	3 (2 to 4)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at rest at 72 hours

End point title	Pain intensity (NRS, 010) at rest at 72 hours
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at rest and at 72 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	3 (1 to 3)	1 (0 to 3)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pain intensity (NRS, 010) at coughing at 72 hours

End point title	Pain intensity (NRS, 010) at coughing at 72 hours
End point description:	
End point type	Other pre-specified
End point timeframe:	
Pain intensity (NRS, 010) at coughing at 72 hours	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: NRS, 0-10				
median (inter-quartile range (Q1-Q3))	4 (2 to 6)	4 (3 to 6)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: ASA physical status

End point title	ASA physical status
End point description:	
End point type	Other pre-specified
End point timeframe:	
Preoperatively	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
"1"	29	26		
"2"	31	36		
"3"	3	1		
Missing	1	0		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Minor laparotomy performed

End point title	Minor laparotomy performed
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n	11	11		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Vasopressor (Ephedrine)

End point title	Vasopressor (Ephedrine)
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End point description:

End point type	Other pre-specified
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End point timeframe:

Intraoperative

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
Vasopressor (Ephedrine)	53	48		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: BMI

End point title	BMI
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End point description:

End point type	Other pre-specified
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End point timeframe:

Preoperative

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: kg/m2				
arithmetic mean (confidence interval 95%)	26.9 (25.7 to 28.0)	27.1 (26.3 to 28.7)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Bleeding

End point title	Bleeding
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: ml				
median (inter-quartile range (Q1-Q3))	50 (20 to 100)	75 (20 to 150)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Uterus weight

End point title	Uterus weight
End point description:	
End point type	Other pre-specified
End point timeframe:	
Interaoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: mg				
median (inter-quartile range (Q1-Q3))	216 (130 to 428)	204 (100 to 401)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Crystalloids

End point title	Crystalloids
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperativ	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: ml				
median (inter-quartile range (Q1-Q3))	1200 (1037 to 1400)	1250 (1100 to 1400)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Propofol

End point title	Propofol
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: ml				
arithmetic mean (confidence interval 95%)	103.8 (95.5 to 112.1)	110.9 (102.5 to 119.4)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Remifentanyl

End point title	Remifentanyl
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: ml				
arithmetic mean (confidence interval 95%)	87.2 (78.7 to 95.7)	93.7 (85.9 to 101.5)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Anaesthesia duration

End point title	Anaesthesia duration
End point description:	
End point type	Other pre-specified
End point timeframe:	
Interaoperative	



End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: min				
median (inter-quartile range (Q1-Q3))	160 (144 to 185)	160 (145 to 190)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Surgery duration

End point title	Surgery duration
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: min				
median (inter-quartile range (Q1-Q3))	108 (90 to 130)	107 (91 to 120)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Time from drug administration to extubation

End point title	Time from drug administration to extubation
End point description:	
End point type	Other pre-specified
End point timeframe:	
Intraoperative	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: min				
median (inter-quartile range (Q1-Q3))	65 (55 to 75)	63 (51 to 77)		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Same-day discharge

End point title	Same-day discharge
End point description:	
End point type	Other pre-specified
End point timeframe:	
During hospitalisation	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
number (not applicable)	47	44		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Reason for overnight stay

End point title	Reason for overnight stay
End point description:	
End point type	Other pre-specified
End point timeframe:	
During hospitalisaation	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: n				
number (not applicable)				
Pain	2	3		
PONV	7	7		
No reason specified	2	2		
Other	6	7		

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Time in hospital

End point title	Time in hospital
End point description:	
End point type	Other pre-specified
End point timeframe:	
During hospitalisation	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: min				
median (inter-quartile range (Q1-Q3))	354 (273 to 998)	394 (318 to 1139)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

4 months

Assessment type	Systematic
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### Dictionary used

Dictionary name	None
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Dictionary version	0
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### Reporting groups

Reporting group title	Intervention
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Reporting group description: -

Reporting group title	Control
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Reporting group description: -

Serious adverse events	Intervention	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 64 (34.38%)	19 / 63 (30.16%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Hospitalisation due to heavy bleeding			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Re-operation after primary surgery due to incomplete closure of the surgical wound			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia during surgery			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Prolonged hospitalisation due to postoperative symptoms			

including PONV, dizziness, low blood pr			
subjects affected / exposed	15 / 64 (23.44%)	12 / 63 (19.05%)	
occurrences causally related to treatment / all	15 / 15	12 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged hospitalisation due to insecurity with discharge			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hospitalisation due to a bleeding gastric ulcer			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation due to pain caused by lack of flatus and bowel movement (sub-ileus)			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Desaturation			
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Prolonged hospitalisation due to lack of urination			
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Admitted to hospital in 3 days after surgery due to pain and fever			

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reoperation due to wound infection			
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	
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: 5 %

<b>Non-serious adverse events</b>	Intervention	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 64 (18.75%)	7 / 63 (11.11%)	
General disorders and administration site conditions			
Outpatient check-up due to bleeding			
subjects affected / exposed	3 / 64 (4.69%)	2 / 63 (3.17%)	
occurrences (all)	5	2	
Outpatient check-up due to postoperative symptoms	Additional description: Outpatient check-up due to postoperative symptoms e.g. questions regarding bandage		
subjects affected / exposed	4 / 64 (6.25%)	4 / 63 (6.35%)	
occurrences (all)	7	4	
Outpatient check-up due to postoperative pain			
subjects affected / exposed	3 / 64 (4.69%)	1 / 63 (1.59%)	
occurrences (all)	3	3	
Outpatient check-up of sutur			
subjects affected / exposed	2 / 64 (3.13%)	0 / 63 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Postoperative infection			
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	

## 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

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/37638073>