# 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 |

**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 |
| **Arm title** | 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.

| | |
|---|---|
| **Arm title** | Control |

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.

| **Number of subjects in period 1** | 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 |
| 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. | |

| Reporting group values | Intervention | Control | Total |
|---|---|---|---|
| Number of subjects | 81 | 82 | 163 |
| Age categorical<br>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<br>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 |

End point description:

| End point type | Primary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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

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

| End point title | Pain intensity (NRS, 010) at rest at 6 hours |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Pain intensity (NRS, 010) at rest 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)) | 2 (1 to 3) | 2 (1 to 3) | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Pain intensity (NRS, 010) at rest at 24 hours |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Pain intensity (NRS, 010) at rest at24 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) | 2 (1 to 4) | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Pain intensity (NRS, 010) at rest at 48 hours |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

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) |
|---|---|

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 | | | | |
| Vasopressor (Ephedrine) | 53 | 48 | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: BMI

| End point title | BMI |
|---|---|

End point description:

| End point type | Other pre-specified |
|---|---|

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: Remifentanil

| End point title | Remifentanil |
|---|---|

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 |

| Dictionary used | |
|---|---|
| Dictionary name | None |
| Dictionary version | 0 |

| Reporting groups | |
|---|---|
| Reporting group title | Intervention |
| Reporting group description: - | |
| Reporting group title | Control |
| 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 postoperoperative symprtoms | | | |

| | | | |
|---|---|---|---|
| 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 %

| **Non-serious adverse events** | 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

### 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/37638073