



Clinical trial results:

Effect of Combinations of Paracetamol, Ibuprofen, and Dexamethasone on Patient-Controlled Morphine Consumption in the First 24 Hours After Total Hip Arthroplasty. The RECIPE Randomized Clinical Trial Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-002844-25 |
| Trial protocol | DK |
| Global end of trial date | 15 February 2023 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 16 October 2024 |
| First version publication date | 16 October 2024 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | SM1-JOAST-2019 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04123873 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | RCAI, Department of Anaesthesiology, Næstved-Slagelse-Ringsted Hospitals |
| Sponsor organisation address | Ringstedgade 61, Næstved, Denmark, 4700 |
| Public contact | Dept of Anaesthesiology, Næstved Hospital, 0045 56514002, anaestesisekretariat@regionsjaelland.dk |
| Scientific contact | Dept of Anaesthesiology, Næstved Hospital, 0045 56514002, anaestesisekretariat@regionsjaelland.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 | 15 February 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 February 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 February 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To investigate the analgesic effects, by differences in 24-hour morphine consumption, of different combinations of paracetamol, ibuprofen, and dexamethasone after total hip arthroplasty.

Protection of trial subjects:

Subjects received a Patient Controlled Analgesia Pump with morphine, where they could steer their own pain treatment. Thus reducing patients discomfort in trial

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 January 2020 |
| 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 | Denmark: 1060 |
| Worldwide total number of subjects | 1060 |
| EEA total number of subjects | 1060 |

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) | 348 |
| From 65 to 84 years | 680 |
| 85 years and over | 32 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants scheduled for primary, unilateral total hip arthroplasty were screened for enrolment. 4468 patients were assessed for eligibility.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Paracetamol plus ibuprofen plus dexamthasone |

Arm description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Paracetamol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively.

| | |
|--|-----------|
| Investigational medicinal product name | Ibuprofen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively.

| | |
|--|------------------------|
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or afterthe induction of general anaesthesia.

| | |
|---|---------------------------------|
| Arm title | Ibuprofen plus dexamthasone |
| Arm description: Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol. | |
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |
| Dosage and administration details: Oral placebo 1000 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. | |
| Investigational medicinal product name | Ibuprofen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively. | |
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or afterthe induction of general anaesthesia. | |
| Arm title | Paracetamol plus dexatmethasone |
| Arm description: Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen. | |
| Arm type | Experimental |
| Investigational medicinal product name | Paracetamol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively. | |
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|------------------------|
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dexamthasone 24 mg was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

| | |
|--|----------------------|
| Investigational medicinal product name | Placebo to Ibuprofen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Oral placebo 400 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively.

| | |
|------------------|----------------------------|
| Arm title | Paracetamol plus Ibuprofen |
|------------------|----------------------------|

Arm description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Paracetamol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The first dose of oral medication 1000 mg was given as premedication 1 h before surgery. The three remaining doses (1000 mg each) were continued postoperatively with 6 h intervals until 24 h postoperatively.

| | |
|--|-----------|
| Investigational medicinal product name | Ibuprofen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The first dose of oral medication 400 mg was given as premedication 1 h before surgery. The three remaining doses (each 400 mg) were continued postoperatively with 6 h intervals until 24 h postoperatively.

| | |
|--|--------------------------|
| Investigational medicinal product name | Placebo to Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

The intravenous placebo (sodium chloride 6 ml) was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

| Number of subjects in period 1 | Paracetamol plus ibuprofen plus dexamthasone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone |
|------------------------------------|--|--------------------------------|----------------------------------|
| | | | |
| Started | 265 | 265 | 265 |
| Completed | 258 | 262 | 262 |
| Not completed | 7 | 3 | 3 |
| Consent withdrawn by subject | - | - | 1 |
| Physician decision | - | - | 2 |
| Expiration of interventional drugs | 1 | 1 | - |
| Surgery cancelled | 5 | 2 | - |
| Trial personnel overlooked surgery | 1 | - | - |

| Number of subjects in period 1 | Paracetamol plus Ibuprofen |
|------------------------------------|-------------------------------|
| Started | 265 |
| Completed | 261 |
| Not completed | 4 |
| Consent withdrawn by subject | 2 |
| Physician decision | 1 |
| Expiration of interventional drugs | - |
| Surgery cancelled | 1 |
| Trial personnel overlooked surgery | - |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Paracetamol plus ibuprofen plus dexamthesone |
| Reporting group description: Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia. | |
| Reporting group title | Ibuprofen plus dexamthasone |
| Reporting group description: Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol. | |
| Reporting group title | Paracetamol plus dexatmethasone |
| Reporting group description: Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen. | |
| Reporting group title | Paracetamol plus Ibuprofen |
| Reporting group description: Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone. | |

| Reporting group values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone |
|---|--|-----------------------------|---------------------------------|
| Number of subjects | 265 | 265 | 265 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years median inter-quartile range (Q1-Q3) | 69 62 to 74 | 69 60 to 75 | 69 61 to 76 |
| Gender categorical Units: Subjects | | | |
| Female | 148 | 141 | 153 |
| Male | 117 | 124 | 112 |
| American Society of Anesthesiologists score Units: Subjects | | | |
| Healthy | 64 | 67 | 58 |
| Mild systemic disease | 171 | 168 | 179 |

| | | | |
|--|-----|-----|-----|
| Severe systemic disease | 30 | 30 | 28 |
| Diabetes | | | |
| Units: Subjects | | | |
| Type 2 diabetes | 16 | 8 | 18 |
| No diabetes | 249 | 257 | 247 |
| Use of paracetamol before surgery | | | |
| Units: Subjects | | | |
| None | 40 | 39 | 36 |
| As needed | 111 | 101 | 105 |
| Daily use | 114 | 125 | 124 |
| Use of NSAID before surgery | | | |
| Units: Subjects | | | |
| None | 117 | 131 | 128 |
| As needed | 96 | 79 | 79 |
| Daily use | 52 | 55 | 58 |
| Daily opioid users: type of opioid | | | |
| Units: Subjects | | | |
| Morphine | 6 | 8 | 4 |
| Oxycodone | 4 | 4 | 6 |
| Tramadol | 6 | 5 | 7 |
| None | 249 | 248 | 248 |
| Use of gabapentinoids before surgery | | | |
| Units: Subjects | | | |
| None | 255 | 252 | 255 |
| As needed | 0 | 4 | 3 |
| Daily use | 10 | 9 | 7 |
| Use of antidepressants before surgery | | | |
| Units: Subjects | | | |
| None | 245 | 251 | 253 |
| As needed | 0 | 0 | 0 |
| Daily use | 13 | 11 | 9 |
| Unknown | 7 | 3 | 3 |
| Surgery type | | | |
| Units: Subjects | | | |
| Uncemented | 206 | 204 | 204 |
| Hybrid | 35 | 36 | 33 |
| Cemented | 21 | 21 | 23 |
| Not registered | 3 | 4 | 5 |
| Anaesthesia method | | | |
| Units: Subjects | | | |
| Spinal | 194 | 202 | 203 |
| General anaesthesia | 58 | 48 | 49 |
| Conversion from spinal to general anaesthesia | 13 | 15 | 13 |
| Spinal type plain | | | |
| Units: Subjects | | | |
| Spinal type plain | 202 | 214 | 213 |
| No spinal | 63 | 51 | 52 |
| Sufentanil administrated | | | |
| Sufentanil administrated for participants in general | | | |

| | | | |
|--|---------------|------------------|---------------|
| anaesthesia (planned or converted from spinal) | | | |
| Units: Subjects | | | |
| Sufentanil administrated | 54 | 48 | 53 |
| No sufentanil administrated | 211 | 217 | 212 |
| Ondansetron administrated | | | |
| Ondansetron 4 mg administrated | | | |
| Units: Subjects | | | |
| Ondansetron administrated | 252 | 254 | 251 |
| No ondansetron adminstrated | 13 | 11 | 14 |
| Perioperative local infiltration analgesia | | | |
| Units: Subjects | | | |
| Perioperative local infiltration analgesia | 0 | 0 | 0 |
| None | 265 | 265 | 265 |
| Height | | | |
| Units: centimetre | | | |
| arithmetic mean | 172.1 | 172.2 | 171.6 |
| standard deviation | ± 8.9 | ± 8.1 | ± 9.2 |
| Weigth | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | 82 | 79.8 | 80.9 |
| standard deviation | ± 17.4 | ± 15.5 | ± 15.5 |
| BMI | | | |
| Units: kilogram(s)/square metre | | | |
| arithmetic mean | 27.4 | 26.8 | 27.4 |
| standard deviation | ± 4.6 | ± 4.2 | ± 4.2 |
| Morphine users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 10.0 | 10.0 | 20.0 |
| inter-quartile range (Q1-Q3) | 10.0 to 11.5 | 10.0 to 16.3 | 20.0 to 22.5 |
| Oxycodone users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 20.0 | 10.0 | 20.0 |
| inter-quartile range (Q1-Q3) | 16.3 to 22.5 | 8.8 to 15.0 | 12.5 to 20.0 |
| Tramadol users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 75.0 | 100.0 | 100.0 |
| inter-quartile range (Q1-Q3) | 50.0 to 100.0 | 100.00 to 100.00 | 50.0 to 125.0 |
| Pain at rest VAS | | | |
| Units: millimetre(s) | | | |
| median | 20.0 | 20.0 | 17.0 |
| inter-quartile range (Q1-Q3) | 1.5 to 40.0 | 4.8 to 35.0 | 2.5 to 35.0 |
| Pain during mobilisation VAS | | | |
| Units: millimetre | | | |
| median | 45.5 | 44.0 | 41.0 |
| inter-quartile range (Q1-Q3) | 21.0 to 70.0 | 20.0 to 65.5 | 20.0 to 64.0 |
| Surgery duration | | | |
| Units: minute | | | |
| median | 55 | 55 | 55 |
| inter-quartile range (Q1-Q3) | 45 to 68 | 45 to 69 | 45 to 69 |
| Bupivacaine dose | | | |

| | | | |
|---|--------------|--------------|--------------|
| Units: milligram(s) | | | |
| median | 12.0 | 12.5 | 12.5 |
| inter-quartile range (Q1-Q3) | 11.0 to 12.5 | 11.0 to 12.5 | 11.0 to 12.5 |
| Sufentanil dose | | | |
| Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal) | | | |
| Sufentanil dose | | | |
| Units: microgram(s) | | | |
| median | 22.5 | 22.8 | 22.5 |
| inter-quartile range (Q1-Q3) | 19.0 to 27.3 | 20.0 to 26.4 | 20.0 to 26.9 |
| Blood loss | | | |
| Units: millilitre(s) | | | |
| median | 300 | 300 | 250 |
| inter-quartile range (Q1-Q3) | 200 to 443 | 200 to 440 | 175 to 400 |

| Reporting group values | Paracetamol plus Ibuprofen | Total | |
|---|-------------------------------|-------|--|
| Number of subjects | 265 | 1060 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 70 | | |
| inter-quartile range (Q1-Q3) | 62 to 76 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 156 | 598 | |
| Male | 109 | 462 | |
| American Society of Anesthesiologists score | | | |
| Units: Subjects | | | |
| Healthy | 56 | 245 | |
| Mild systemic disease | 182 | 700 | |
| Severe systemic disease | 27 | 115 | |
| Diabetes | | | |
| Units: Subjects | | | |
| Type 2 diabetes | 12 | 54 | |
| No diabetes | 253 | 1006 | |
| Use of paracetamol before surgery | | | |
| Units: Subjects | | | |
| None | 45 | 160 | |
| As needed | 94 | 411 | |
| Daily use | 126 | 489 | |

| | | | |
|---|-----|------|--|
| Use of NSAID before surgery | | | |
| Units: Subjects | | | |
| None | 123 | 499 | |
| As needed | 76 | 330 | |
| Daily use | 66 | 231 | |
| Daily opioid users: type of opioid | | | |
| Units: Subjects | | | |
| Morphine | 7 | 25 | |
| Oxycodone | 6 | 20 | |
| Tramadol | 7 | 25 | |
| None | 245 | 990 | |
| Use of gabapentinoids before surgery | | | |
| Units: Subjects | | | |
| None | 255 | 1017 | |
| As needed | 2 | 9 | |
| Daily use | 8 | 34 | |
| Use of antidepressants before surgery | | | |
| Units: Subjects | | | |
| None | 252 | 1001 | |
| As needed | 1 | 1 | |
| Daily use | 8 | 41 | |
| Unknown | 4 | 17 | |
| Surgery type | | | |
| Units: Subjects | | | |
| Uncemented | 209 | 823 | |
| Hybrid | 32 | 136 | |
| Cemented | 18 | 83 | |
| Not registered | 6 | 18 | |
| Anaesthesia method | | | |
| Units: Subjects | | | |
| Spinal | 187 | 786 | |
| General anaesthesia | 59 | 214 | |
| Conversion from spinal to general anaesthesia | 19 | 60 | |
| Spinal type plain | | | |
| Units: Subjects | | | |
| Spinal type plain | 203 | 832 | |
| No spinal | 62 | 228 | |
| Sufentanil administrated | | | |
| Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal) | | | |
| Units: Subjects | | | |
| Sufentanil administrated | 61 | 216 | |
| No sufentanil administrated | 204 | 844 | |
| Ondansetron administrated | | | |
| Ondansetron 4 mg administrated | | | |
| Units: Subjects | | | |
| Ondansetron administrated | 250 | 1007 | |
| No ondansetron administrated | 15 | 53 | |
| Perioperative local infiltration analgesia | | | |

| | | | |
|---|----------------|------|--|
| Units: Subjects | | | |
| Perioperative local infiltration analgesia | 1 | 1 | |
| None | 264 | 1059 | |
| Height | | | |
| Units: centimetre | | | |
| arithmetic mean | 171.7 | | |
| standard deviation | ± 9.4 | - | |
| Weighth | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | 81.6 | | |
| standard deviation | ± 17.0 | - | |
| BMI | | | |
| Units: kilogram(s)/square metre | | | |
| arithmetic mean | 27.6 | | |
| standard deviation | ± 4.5 | - | |
| Morphine users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 10.0 | | |
| inter-quartile range (Q1-Q3) | 10.0 to 15.0 | - | |
| Oxycodone users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 10.0 | | |
| inter-quartile range (Q1-Q3) | 6.3 to 13.8 | - | |
| Tramadol users: daily dose, mg | | | |
| Units: milligram(s) | | | |
| median | 100.0 | | |
| inter-quartile range (Q1-Q3) | 100.0 to 100.0 | - | |
| Pain at rest VAS | | | |
| Units: millimetre(s) | | | |
| median | 19.0 | | |
| inter-quartile range (Q1-Q3) | 0.0 to 40.0 | - | |
| Pain during mobilisation VAS | | | |
| Units: millimetre | | | |
| median | 46.0 | | |
| inter-quartile range (Q1-Q3) | 20.0 to 69.0 | - | |
| Surgery duration | | | |
| Units: minute | | | |
| median | 55 | | |
| inter-quartile range (Q1-Q3) | 45 to 70 | - | |
| Bupivacaine dose | | | |
| Units: milligram(s) | | | |
| median | 12.5 | | |
| inter-quartile range (Q1-Q3) | 11.0 to 12.5 | - | |
| Sufentanil dose | | | |
| Sufentanil administrated for participants in general anaesthesia (planned or converted from spinal) | | | |
| Sufentanil dose | | | |
| Units: microgram(s) | | | |
| median | 25.0 | | |
| inter-quartile range (Q1-Q3) | 20.0 to 27.0 | - | |
| Blood loss | | | |
| Units: millilitre(s) | | | |

| | | | |
|------------------------------|------------|---|--|
| median | 300 | | |
| inter-quartile range (Q1-Q3) | 200 to 494 | - | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Paracetamol plus ibuprofen plus dexamthasone |
| Reporting group description: Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia. | |
| Reporting group title | Ibuprofen plus dexamthasone |
| Reporting group description: Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol. | |
| Reporting group title | Paracetamol plus dexatmethasone |
| Reporting group description: Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen. | |
| Reporting group title | Paracetamol plus Ibuprofen |
| Reporting group description: Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone. | |

Primary: 24-h morphine consumption

| | |
|---|---------------------------|
| End point title | 24-h morphine consumption |
| End point description: | |
| End point type | Primary |
| End point timeframe: Morphine consumption from last suture to 24 hours after last suture | |

| End point values | Paracetamol plus ibuprofen plus dexamthasone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: milligram(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 15 (8 to 26) | 16 (10 to 30) | 20 (12 to 32) | 24 (12 to 38) |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Median difference |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus ibuprofen plus dexamthasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.14 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | 2 |

| | |
|---|--|
| Statistical analysis title | Median difference |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0013 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -4 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | -1 |

| | |
|---|---|
| Statistical analysis title | Median difference |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -6 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | -3 |

| | |
|---|---|
| Statistical analysis title | Median difference |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.033 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Median difference |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -4.5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | -2 |

| | |
|---|--|
| Statistical analysis title | Median difference |
| Comparison groups | Paracetamol plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 2 |

Secondary: Adverse events, 0 to 24 h postoperatively

| | |
|-----------------|---|
| End point title | Adverse events, 0 to 24 h postoperatively |
|-----------------|---|

End point description:

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

End point timeframe:

0 to 24 hours postoperatively

| End point values | Paracetamol plus ibuprofen plus dexamthasone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|-----------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: events | 91 | 99 | 103 | 165 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Relative Risk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.55 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 1.14 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Relative Risk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|--------------------|
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.34 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 1.15 |

| | |
|---|---|
| Statistical analysis title | Relative Risk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 0.66 |

| | |
|---|---|
| Statistical analysis title | Relative Risk |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.73 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.22 |

| | |
|---|--|
| Statistical analysis title | Relative Risk |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.7 |

| | |
|---|---|
| Statistical analysis title | Relative Risk |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 0.73 |

| | |
|---|---------------------------------------|
| Secondary: Pain at rest 24 hours postoperatively | |
| End point title | Pain at rest 24 hours postoperatively |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 10 (1 to 20) | 12 (0 to 28) | 13 (1 to 25) | 12 (1 to 25) |

Statistical analyses

| Statistical analysis title | Pairwise comparisons between the median pain score |
|---|--|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0 |

| Statistical analysis title | Pairwise comparisons between the median pain score |
|---|--|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0 |

| Statistical analysis title | Pairwise comparisons between the median pain score |
|-----------------------------------|---|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.14 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons between the median pain score |
| Comparison groups | Paracetamol plus dexamethasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.72 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 1 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons between the median pain score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.72 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 1 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons between the median |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.92 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 2 |

Secondary: Pain during mobilisation at 24 h postoperatively

| | |
|--------------------------|--|
| End point title | Pain during mobilisation at 24 h postoperatively |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|---------------------------------------|---|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 31 (18 to 50) | 32 (18 to 50) | 40 (20 to 60) | 43 (27 to 65) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 5 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0031 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -6 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | 0 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -10 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -16 |
| upper limit | -5 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.016 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -10 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -15 |
| upper limit | -4 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons pain score mobilisation |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.058 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 2 |

Secondary: Maximum pain during 5 m walk

| | |
|-----------------|------------------------------|
| End point title | Maximum pain during 5 m walk |
|-----------------|------------------------------|

End point description:

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

End point timeframe:

24 h postoperatively

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 27 (15 to 41) | 30 (16 to 46) | 35 (20 to 50) | 35 (20 to 51) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons max pain score walk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -3 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | 2 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons max pain score walk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -6 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | -1 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons max pain score walk |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -9 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | 3 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons max pain score walk |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.078 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -3 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -9 |
| upper limit | 2 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Pairwise comparisons max pain score walk |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.016 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|---|---|
| Statistical analysis title | Copy of Pairwise comparisons max pain score walk |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.37 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -2 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | 4 |

Other pre-specified: Pain at rest 6h

| | |
|-------------------------|---------------------|
| End point title | Pain at rest 6h |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 6 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamethasone | Paracetamol plus dexamethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|---|------------------------------|--------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 16 (10 to 31) | 20 (8 to 30) | 25 (10 to 40) | 29 (11 to 48) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.73 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | 3 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0076 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -10 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | -4 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0048 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -10 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | -4 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons pain rest 6h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.032 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -4 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

Other pre-specified: Pain during mobilisation, 6 h

| | |
|-------------------------|-------------------------------|
| End point title | Pain during mobilisation, 6 h |
| End point description: | |
| | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 6 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|---------------------------------------|---|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 30 (15 to 51) | 30 (15 to 50) | 37 (20 to 55) | 48 (25 to 69) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.32 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 7 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 1 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -13 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -20 |
| upper limit | -6 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.02 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -11 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -15 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -20 |
| upper limit | -8 |

| | |
|---|---|
| Statistical analysis title | Pairwise comparisons pain mobilisation 6h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -9 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | -15 |
| upper limit | -2 |

Other pre-specified: Nausea, 6 h

| | |
|-------------------------|---------------------|
| End point title | Nausea, 6 h |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 6 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamthessone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|-----------------------------|---|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 248 | 251 | 244 | 243 |
| Units: patients | 21 | 19 | 23 | 49 |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthessone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 499 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.71 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.46 |
| upper limit | 1.78 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthessone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 492 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.68 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.89 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.56 |
| upper limit | 2.02 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 491 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 0.63 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 495 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.041 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 1.83 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |

| | |
|---|--------------------|
| Number of subjects included in analysis | 494 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.19 |
| upper limit | 0.57 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 6h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 487 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0012 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 0.69 |

Other pre-specified: Nausea 24 h

| | |
|--------------------------|---------------------|
| End point title | Nausea 24 h |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamethasone | Paracetamol plus dexamethasone | Paracetamol plus Ibuprofen |
|-----------------------------|---|------------------------------|--------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 256 | 261 | 257 | 257 |
| Units: patients | 49 | 68 | 70 | 125 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 517 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.058 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.97 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexammethasone |
| Number of subjects included in analysis | 513 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.03 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 1.02 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|--------------------|
| Number of subjects included in analysis | 513 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.39 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.28 |
| upper limit | 0.5 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 518 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.76 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 1.33 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 518 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 0.67 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Nausea 24h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 514 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 0.69 |

Other pre-specified: Vomiting 0-24 h

| | |
|-------------------------------|---------------------|
| End point title | Vomiting 0-24 h |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 0 to 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|-----------------------------|---|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 256 | 261 | 255 | 257 |
| Units: patients | 23 | 29 | 33 | 81 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 517 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.42 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.81 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.39 |
| upper limit | 1.22 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 511 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.16 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.39 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 513 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.16 |
| upper limit | 0.41 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|--------------------|
| Number of subjects included in analysis | 516 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.52 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.6 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 518 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.22 |
| upper limit | 0.49 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Vomiting 0-24h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 512 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 0.56 |

Other pre-specified: Dizziness walk test, 24 h

| | |
|-----------------|---------------------------|
| End point title | Dizziness walk test, 24 h |
|-----------------|---------------------------|

End point description:

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

End point timeframe:

24 hours postoperatively

| End point values | Paracetamol plus ibuprofen plus dexamthessone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|-----------------------------|---|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 233 | 237 | 230 | 221 |
| Units: Patients | 27 | 33 | 25 | 48 |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthessone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 470 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.47 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 1.23 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthessone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 463 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.78 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 1.07 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 2.18 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 454 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0042 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.31 |
| upper limit | 0.77 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 467 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.34 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 1.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 2.46 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |

| | |
|---|--------------------|
| Number of subjects included in analysis | 458 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.029 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.39 |
| upper limit | 0.9 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Dizziness walk test 24h |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 451 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0023 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 0.73 |

Other pre-specified: Anti-emetic use, 0–24 h

| | |
|-------------------------------|-------------------------|
| End point title | Anti-emetic use, 0–24 h |
| End point description: | |
| | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 0 to 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamethasone | Paracetamol plus dexamethasone | Paracetamol plus Ibuprofen |
|-----------------------------|---|------------------------------|--------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 257 | 261 | 261 | 263 |
| Units: patients | 36 | 49 | 65 | 95 |

Statistical analyses

| Statistical analysis title | Relative Risk Anti-emetic use |
|---|--|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 518 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 1.03 |

| Statistical analysis title | Relative Risk Anti-emetic use |
|---|--|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 518 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0017 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.41 |
| upper limit | 0.89 |

| Statistical analysis title | Relative Risk Anti-emetic use |
|----------------------------|---|
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|--------------------|
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.51 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Anti-emetic use |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 522 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.089 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 1.12 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Anti-emetic use |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.37 |
| upper limit | 0.67 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Anti-emetic use |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0037 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.86 |

Other pre-specified: Sleep quality

| | |
|---------------------------------|---------------------|
| End point title | Sleep quality |
| End point description: | |
| VAS 0-100, 0 worst to 100 best. | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 24 hours postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|---------------------------------------|---|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 50 (30 to 79) | 50 (30 to 80) | 50 (30 to 75) | 58 (40 to 80) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.65 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 4 |

| | |
|---|--|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 6 |

| | |
|---|---|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.51 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.27 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 8 |

| | |
|---|--|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Median difference sleep quality |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0073 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11 |
| upper limit | -1 |

Other pre-specified: Intra-operative blood loss

| | |
|-----------------|----------------------------|
| End point title | Intra-operative blood loss |
|-----------------|----------------------------|

End point description:

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

End point timeframe:

Intra-operative blood loss

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millilitre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 300 (200 to 450) | 300 (200 to 440) | 250 (175 to 400) | 300 (200 to 500) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.77 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 50 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.13 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | 20 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 50 |

| | |
|---|---|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.26 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -50 |
| upper limit | 0 |

| | |
|---|---|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.044 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | 40 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 60 |

| | |
|---|--|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.46 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -50 |
| upper limit | 25 |

| | |
|---|---|
| Statistical analysis title | Median difference blood loss |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.011 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (net) |
| Point estimate | -50 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -75 |
| upper limit | 0 |

| | |
|---|---------------------------------------|
| Other pre-specified: Serious adverse events within 90 days | |
| End point title | Serious adverse events within 90 days |
| End point description: | |
| | |
| End point type | Other pre-specified |
| End point timeframe: | |
| Within 90 days postoperatively. | |

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|-----------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: patients | 20 | 24 | 31 | 35 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.58 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.37 |
| upper limit | 1.33 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.12 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.38 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|--------------------|
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.036 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.28 |
| upper limit | 0.88 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.32 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 1.54 |

| | |
|---|--|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.12 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.35 |
| upper limit | 1.01 |

| | |
|---|---|
| Statistical analysis title | Relative Risk Adverse events 90 days |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.55 |
| Method | Regression, Linear |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.26 |

Other pre-specified: Oxford Hip Score at 90 days

| | |
|-------------------------|-----------------------------|
| End point title | Oxford Hip Score at 90 days |
| End point description: | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 90 days postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamethasone | Ibuprofen plus dexamthasone | Paracetamol plus dexammethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|---|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: points | | | | |
| median (inter-quartile range (Q1-Q3)) | 41 (36 to 450) | 41 (36 to 45) | 41 (34 to 45) | 42 (36 to 45) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.52 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1 |

| | |
|---|--|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.14 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 2 |

| | |
|---|---|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.99 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexatmethasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.49 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 2 |

| | |
|---|--|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.74 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1 |

| | |
|---|---|
| Statistical analysis title | Median difference Oxford Hip Score |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.34 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 0 |

Other pre-specified: EQ5D5L index score

| | |
|-----------------|--------------------|
| End point title | EQ5D5L index score |
|-----------------|--------------------|

| |
|------------------------|
| End point description: |
|------------------------|

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

| |
|----------------------|
| End point timeframe: |
|----------------------|

| |
|-------------------------|
| 90 days postoperatively |
|-------------------------|

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|---------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: score | | | | |
| median (inter-quartile range (Q1-Q3)) | 0.93 (0.87 to 1) | 0.93 (0.88 to 1) | 0.93 (0.87 to 1) | 0.93 (0.87 to 1) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.78 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.004 |
| upper limit | 0 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexatmethasone |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.68 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.005 |

| | |
|---|---|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.77 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|---|---|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.56 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.008 |

| | |
|---|--|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.58 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.004 |

| | |
|---|---|
| Statistical analysis title | Median difference EQ5D5L index score |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.91 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.002 |

| | |
|--|--------------------------|
| Other pre-specified: EQ5D5L VAS score 90 days | |
| End point title | EQ5D5L VAS score 90 days |
| End point description: | |
| | |
| End point type | Other pre-specified |
| End point timeframe: | |
| 90 days postoperatively | |

| End point values | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexamthasone | Paracetamol plus Ibuprofen |
|---------------------------------------|--|-----------------------------|-------------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 258 | 262 | 262 | 261 |
| Units: millimetre(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 85 (75 to 90) | 85 (75 to 90) | 85 (75 to 90) | 85 (75 to 90) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Ibuprofen plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.71 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 3 |

| | |
|---|--|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 520 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.75 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 2 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Paracetamol plus ibuprofen plus dexamthesone v Paracetamol plus Ibuprofen |

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 519 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.59 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 3 |

| | |
|---|---|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus dexamthasone |
| Number of subjects included in analysis | 524 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.48 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 5 |

| | |
|---|--|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Ibuprofen plus dexamthasone v Paracetamol plus Ibuprofen |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.86 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|---|---|
| Statistical analysis title | Median difference EQ5D5L VAS score |
| Comparison groups | Paracetamol plus Ibuprofen v Paracetamol plus dexamethasone |
| Number of subjects included in analysis | 523 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.46 |
| Method | Hodges-Lehmann |
| Parameter estimate | Median difference (final values) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 0 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

0 to 24 hours postoperatively

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|---------|
| Dictionary name | ICH-GCP |
|-----------------|---------|

| | |
|--------------------|------------|
| Dictionary version | Revision 2 |
|--------------------|------------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Paracetamol plus ibuprofen plus dexamthasone |
|-----------------------|--|

Reporting group description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg. The first dose of oral medication was given as premedication 1 h before surgery. The three remaining doses were continued postoperatively with 6 h intervals until 24 h postoperatively. The intravenous medication was given immediately after the onset of spinal anaesthesia or after the induction of general anaesthesia.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Ibuprofen plus dexamthasone |
|-----------------------|-----------------------------|

Reporting group description:

Oral ibuprofen 400 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching paracetamol.

| | |
|-----------------------|---------------------------------|
| Reporting group title | Paracetamol plus dexatmethasone |
|-----------------------|---------------------------------|

Reporting group description:

Oral paracetamol 1000 mg plus single-dose intravenous dexamethasone 24 mg plus placebo matching ibuprofen.

| | |
|-----------------------|----------------------------|
| Reporting group title | Paracetamol plus Ibuprofen |
|-----------------------|----------------------------|

Reporting group description:

Oral paracetamol 1000 mg plus oral ibuprofen 400 mg plus placebo matching dexamethasone.

| Serious adverse events | Paracetamol plus ibuprofen plus dexamthasone | Ibuprofen plus dexamthasone | Paracetamol plus dexatmethasone |
|---|--|-----------------------------|---------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 258 (2.33%) | 5 / 262 (1.91%) | 3 / 262 (1.15%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Cardiac arrhythmia | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 1 / 262 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemodynamic instability | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Surgical and medical procedures | | | |
| Complete and incomplete prosthetic dislocation | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 1 / 262 (0.38%) | 1 / 262 (0.38%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Neuropathic pain | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drop foot | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Worsening of known symptoms from previous critical illness | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hospitalisation 4 or more days | | | |
| subjects affected / exposed | 3 / 258 (1.16%) | 3 / 262 (1.15%) | 1 / 262 (0.38%) |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Paracetamol plus Ibuprofen | | |
|--|-------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 261 (4.98%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Cardiac arrhythmia | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemodynamic instability | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Complete and incomplete prosthetic dislocation | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Neuropathic pain | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drop foot | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Worsening of known symptoms from previous critical illness | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hospitalisation 4 or more days | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 7 / 261 (2.68%) | | |
| occurrences causally related to treatment / all | 7 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Paracetamol plus ibuprofen plus dexamthesone | Ibuprofen plus dexamthasone | Paracetamol plus dexamtmethasone |
|---|--|--------------------------------|-------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 122 / 258 (47.29%) | 150 / 262 (57.25%) | 167 / 262 (63.74%) |
| Cardiac disorders | | | |
| Vasovagal episode or syncope | | | |
| subjects affected / exposed | 8 / 258 (3.10%) | 1 / 262 (0.38%) | 5 / 262 (1.91%) |
| occurrences (all) | 8 | 1 | 5 |
| Cardiac arrhythmia | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 262 (0.00%) | 1 / 262 (0.38%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypotensive episode | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 1 / 262 (0.38%) |
| occurrences (all) | 0 | 1 | 1 |
| Surgical and medical procedures | | | |
| Blood transfusion | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 2 / 262 (0.76%) | 4 / 262 (1.53%) |
| occurrences (all) | 0 | 2 | 4 |
| Blood oozing from surgical wound | | | |

| | | | |
|--|-------------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 1 / 262 (0.38%) 1 | 2 / 262 (0.76%) 2 |
| Perioperative fracture subjects affected / exposed occurrences (all) | 1 / 258 (0.39%) 1 | 0 / 262 (0.00%) 0 | 2 / 262 (0.76%) 2 |
| Haematoma subjects affected / exposed occurrences (all) | 1 / 258 (0.39%) 1 | 0 / 262 (0.00%) 0 | 0 / 262 (0.00%) 0 |
| Nervous system disorders Dizziness during 5 m walk subjects affected / exposed occurrences (all) | 27 / 258 (10.47%) 27 | 33 / 262 (12.60%) 33 | 25 / 262 (9.54%) 25 |
| Confusion subjects affected / exposed occurrences (all) | 1 / 258 (0.39%) 1 | 1 / 262 (0.38%) 1 | 1 / 262 (0.38%) 1 |
| Delirium subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 0 / 262 (0.00%) 0 | 0 / 262 (0.00%) 0 |
| Worsening of known neurologic symptoms subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 1 / 262 (0.38%) 1 | 0 / 262 (0.00%) 0 |
| Pain and logistics subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 0 / 262 (0.00%) 0 | 0 / 262 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 0 / 262 (0.00%) 0 | 1 / 262 (0.38%) 1 |
| Blood and lymphatic system disorders Non-surgical drop in hemoglobin level subjects affected / exposed occurrences (all) | 0 / 258 (0.00%) 0 | 0 / 262 (0.00%) 0 | 1 / 262 (0.38%) 0 |
| General disorders and administration site conditions Delayed mobilisation or discharge subjects affected / exposed occurrences (all) | 2 / 258 (0.78%) 2 | 7 / 262 (2.67%) 7 | 8 / 262 (3.05%) 8 |

| | | | |
|---|-------------------|-------------------|-------------------|
| Immune system disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 4 / 262 (1.53%) |
| occurrences (all) | 0 | 0 | 4 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 57 / 258 (22.09%) | 70 / 262 (26.72%) | 75 / 262 (28.63%) |
| occurrences (all) | 57 | 70 | 75 |
| Vomiting | | | |
| subjects affected / exposed | 23 / 258 (8.91%) | 29 / 262 (11.07%) | 34 / 262 (12.98%) |
| occurrences (all) | 23 | 29 | 34 |
| Stomach discomfort or pain | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 0 / 262 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 0 / 262 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Desaturation | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 0 / 262 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Impaired kidney function | | | |
| subjects affected / exposed | 1 / 258 (0.39%) | 0 / 262 (0.00%) | 2 / 262 (0.76%) |
| occurrences (all) | 1 | 0 | 2 |
| Urinary infection | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 1 / 262 (0.38%) | 1 / 262 (0.38%) |
| occurrences (all) | 0 | 1 | 1 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 258 (0.00%) | 0 / 262 (0.00%) | 0 / 262 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-------------------------------|--|--|
| Non-serious adverse events | Paracetamol plus Ibuprofen | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 248 / 261 (95.02%) | | |
| Cardiac disorders | | | |

| | | | |
|---|-------------------------|--|--|
| Vasovagal episode or syncope subjects affected / exposed occurrences (all) | 5 / 261 (1.92%) 5 | | |
| Cardiac arrhythmia subjects affected / exposed occurrences (all) | 1 / 261 (0.38%) 1 | | |
| Hypotensive episode subjects affected / exposed occurrences (all) | 3 / 261 (1.15%) 3 | | |
| Surgical and medical procedures | | | |
| Blood transfusion subjects affected / exposed occurrences (all) | 1 / 261 (0.38%) 1 | | |
| Blood oozing from surgical wound subjects affected / exposed occurrences (all) | 0 / 261 (0.00%) 0 | | |
| Perioperative fracture subjects affected / exposed occurrences (all) | 3 / 261 (1.15%) 3 | | |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 261 (0.00%) 0 | | |
| Nervous system disorders | | | |
| Dizziness during 5 m walk subjects affected / exposed occurrences (all) | 48 / 261 (18.39%) 48 | | |
| Confusion subjects affected / exposed occurrences (all) | 1 / 261 (0.38%) 1 | | |
| Delirium subjects affected / exposed occurrences (all) | 1 / 261 (0.38%) 1 | | |
| Worsening of known neurologic symptoms subjects affected / exposed occurrences (all) | 0 / 261 (0.00%) 0 | | |
| Pain and logistics | | | |

| | | | |
|--|--------------------|--|--|
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Non-surgical drop in hemoglobin level | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Delayed mobilisation or discharge | | | |
| subjects affected / exposed | 9 / 261 (3.45%) | | |
| occurrences (all) | 9 | | |
| Immune system disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 133 / 261 (50.96%) | | |
| occurrences (all) | 133 | | |
| Vomiting | | | |
| subjects affected / exposed | 81 / 261 (31.03%) | | |
| occurrences (all) | 81 | | |
| Stomach discomfort or pain | | | |
| subjects affected / exposed | 2 / 261 (0.77%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences (all) | 0 | | |
| Desaturation | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Impaired kidney function | | | |
| subjects affected / exposed | 2 / 261 (0.77%) | | |
| occurrences (all) | 2 | | |
| Urinary infection | | | |
| subjects affected / exposed | 0 / 261 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 261 (0.38%) | | |
| occurrences (all) | 1 | | |

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

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

| |
|---------------|
| None reported |
|---------------|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38458208>