



Clinical trial results:

Epidural ropivacaine as part of a multimodal postoperative pain treatment following thoracolumbar spinal fusion surgery.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-004713-91 |
| Trial protocol | BE |
| Global end of trial date | 06 August 2024 |

Results information

| | |
|-----------------------------------|----------------------------|
| Result version number | v1 (current) |
| This version publication date | 03 May 2025 |
| First version publication date | 03 May 2025 |
| Summary attachment (see zip file) | Article_Tose (25-Tosi.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | ROPISPINE |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | UZ Brussel |
| Sponsor organisation address | Laarbeeklaan, Brussel, Belgium, |
| Public contact | Study Coordinator, UZ Brussel, virgini.vanbuggenhout@uzbrussel.be |
| Scientific contact | Study Coordinator, UZ Brussel, virgini.vanbuggenhout@uzbrussel.be |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 23 October 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 October 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 August 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The goal of this study is to determine if infusion with ropivacaine at a rate of 7 mL/h is an effective additional treatment for postoperative pain after thoracolumbar spinal fusion surgery.

Protection of trial subjects:

Patient safety was assessed during study conduct. During surgery patient was followed by PI, anesthesiologist and surgery team. Afterwards they were followed up by medical staff. At the PACU they had to give pain scores every 10 minutes, in that pain and AE's could be assessed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 December 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 33 |
| Worldwide total number of subjects | 33 |
| EEA total number of subjects | 33 |

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) | 33 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients who were scheduled for thoracic or lumbar posterior interbody fusion surgery between december 2014 and December 2015 were included.

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|----------------------------|----|
| Number of subjects started | 33 |
|----------------------------|----|

| | |
|------------------------------|----|
| Number of subjects completed | 30 |
|------------------------------|----|

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--|
| Reason: Number of subjects | not the right premedication was given: 2 |
|----------------------------|--|

| | |
|----------------------------|---|
| Reason: Number of subjects | problem during surgery, no epidural possible: 1 |
|----------------------------|---|

Period 1

| | |
|----------------|--------------------------------|
| Period 1 title | study conduct (overall period) |
|----------------|--------------------------------|

| | |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

| | |
|-------------------|-------------------------|
| Allocation method | Randomised - controlled |
|-------------------|-------------------------|

| | |
|---------------|-----------------------------|
| Blinding used | Double blind ^[1] |
|---------------|-----------------------------|

| | |
|---------------|--|
| Roles blinded | Subject, Data analyst, Carer, Assessor |
|---------------|--|

Blinding implementation details:

Only PI is not blinded and prepares the medication to be given to the patient, everybody else in the theatre room is blinded. Block randomization was used. All patients scheduled for surgery on a certain day were randomized to the same group.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------------|
| Arm title | placebo group |
|------------------|---------------|

Arm description: -

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|--------|
| Investigational medicinal product name | Saline |
|--|--------|

| | |
|--|--------|
| Investigational medicinal product code | Saline |
|--|--------|

| | |
|------------|--|
| Other name | |
|------------|--|

| | |
|----------------------|-----------------------|
| Pharmaceutical forms | Solution for infusion |
|----------------------|-----------------------|

| | |
|--------------------------|--------------|
| Routes of administration | Epidural use |
|--------------------------|--------------|

Dosage and administration details:

continuous infusion of 0.9% saline

| | |
|------------------|-----------------|
| Arm title | treatment group |
|------------------|-----------------|

Arm description: -

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-------------|
| Investigational medicinal product name | ropivacaine |
|--|-------------|

| | |
|--|-------------|
| Investigational medicinal product code | ropivacaine |
|--|-------------|

| | |
|------------|--|
| Other name | |
|------------|--|

| | |
|----------------------|-----------------------|
| Pharmaceutical forms | Solution for infusion |
|----------------------|-----------------------|

| | |
|--------------------------|--------------|
| Routes of administration | Epidural use |
|--------------------------|--------------|

Dosage and administration details:

continuous infusion of 0.2% ropivacaine during surgery

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Only the PI was not blinded in this study. Everybody else was blinded (patient, anesthesiologist, surgeon,...)

| Number of subjects in period 1[2] | placebo group | treatment group |
|--------------------------------------|---------------|-----------------|
| | | |
| Started | 14 | 16 |
| Completed | 14 | 16 |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 17 patients were included in the placebo group at first, however not the right premedication was given before surgery and for one patient placement of an epidural wasn't possible. Those 3 were excluded from the study. No data was used from them.

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-----------------|
| Reporting group title | placebo group |
| Reporting group description: - | |
| Reporting group title | treatment group |
| Reporting group description: - | |

| Reporting group values | placebo group | treatment group | Total |
|---|---------------|-----------------|-------|
| Number of subjects | 14 | 16 | 30 |
| 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 | | | |
| arithmetic mean | 62 | 55 | |
| standard deviation | ± 16 | ± 18 | - |
| Gender categorical Units: Subjects | | | |
| Female | 7 | 8 | 15 |
| Male | 7 | 8 | 15 |
| ASA class Units: Subjects | | | |
| ASA 1 | 3 | 4 | 7 |
| ASA 2 | 9 | 10 | 19 |
| ASA 3 | 2 | 2 | 4 |
| Weight Units: kilogram(s) | | | |
| arithmetic mean | 70 | 79.8 | |
| standard deviation | ± 12.7 | ± 18.6 | - |
| Height Units: centimetre | | | |
| arithmetic mean | 165.9 | 171.7 | |
| standard deviation | ± 7.7 | ± 11.7 | - |
| BMI Units: kilogram(s)/square metre | | | |
| arithmetic mean | 26.5 | 24.9 | |
| standard deviation | ± 3.7 | ± 10.2 | - |
| preoperative VAS | | | |

| | | | |
|--------------------|-------|-------|---|
| Units: pain score | | | |
| arithmetic mean | 3 | 3.4 | |
| standard deviation | ± 3.1 | ± 2.8 | - |

End points

End points reporting groups

| | |
|--------------------------------|-----------------|
| Reporting group title | placebo group |
| Reporting group description: - | |
| Reporting group title | treatment group |
| Reporting group description: - | |

Primary: VAS Score

| | |
|--|-----------|
| End point title | VAS Score |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| VAS Score were taken at arrival at PACU and then every 10 minutes while still on PACU. VAS score was also measured on day of surgery (day 0), day 1 and day 2. | |

| End point values | placebo group | treatment group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 16 | | |
| Units: pain score | | | | |
| arithmetic mean (standard deviation) | | | | |
| First PACU | 7.2 (± 3.7) | 4.5 (± 3.9) | | |
| mean PACU | 5.7 (± 0.9) | 3.6 (± 3) | | |
| Day 0 | 5 (± 2.9) | 3.5 (± 1.5) | | |
| Day 1 | 2.8 (± 1.5) | 2 (± 0.7) | | |
| Day 2 | 2.1 (± 0.8) | 1.7 (± 1.2) | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | VAS Score |
| Statistical analysis description: | |
| We aimed to detect a 40% reduction in VAS score in the treatment group as compared with the control group. We set type I error $\alpha = 0.05$ (two-sided) and type II error $\beta = 0.2$. For statistical analysis SPSS Statistics® version 23 was used. The normality of the distribution was assessed using Kolmogorov-Smirnov test. The student T-test was used for analysing the differences between the two groups. | |
| Comparison groups | placebo group v treatment group |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 1-sided |
| Parameter estimate | Mean difference (final values) |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |

Primary: Supplemental opioid consumption

| | |
|-----------------|---------------------------------|
| End point title | Supplemental opioid consumption |
|-----------------|---------------------------------|

End point description:

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

End point timeframe:

supplemental opioid consumption was captured in the OR (mg sufentanyl) at the PACU (mg piritramide) and on day 0, day 1 and day 2 (mg oxycodone).

| End point values | placebo group | treatment group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 16 | | |
| Units: milligram(s) | | | | |
| arithmetic mean (standard deviation) | | | | |
| OR | 41.4 (± 14.2) | 55.5 (± 23.5) | | |
| PACU | 14.8 (± 10.9) | 9 (± 7.5) | | |
| Day 0 | 10.5 (± 11.4) | 6.9 (± 7.3) | | |
| Day 1 | 11.4 (± 10.5) | 6.8 (± 7.9) | | |
| Day 2 | 11.8 (± 15.9) | 6 (± 7.5) | | |

Statistical analyses

| | |
|----------------------------|--------------------|
| Statistical analysis title | opioid consumption |
|----------------------------|--------------------|

Statistical analysis description:

Assuming a standard deviation of 2, a minimum of 16 patients per group would be required. We set type I error $\alpha = 0.05$ (two-sided) and type II error $\beta = 0.2$. For statistical analysis SPSS Statistics® version 23 was used. The normality of the distribution was assessed using the Kolmogorov-Smirnov test. The student T-test was used for analysing the differences between the two groups.

| | |
|---|---------------------------------|
| Comparison groups | treatment group v placebo group |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 1-sided |

Secondary: day of mobilization

| | |
|-----------------|---------------------|
| End point title | day of mobilization |
|-----------------|---------------------|

End point description:

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

End point timeframe:

day of mobilization is the day patients started walking again after surgery.

| End point values | placebo group | treatment group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 16 | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Mobilization | 1.5 (± 1) | 0.8 (± 0.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Hospitalization

| | |
|-----------------|-----------------|
| End point title | Hospitalization |
|-----------------|-----------------|

End point description:

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

End point timeframe:

length of stay of hospitalization

| End point values | placebo group | treatment group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 16 | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| hospitalization | 9.6 (± 5.6) | 6.7 (± 3.9) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were captured as from time of signing the ICF till end of the hospitalization.

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

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

Reporting groups

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|-----------------------|---------------|
| Reporting group title | placebo group |
|-----------------------|---------------|

Reporting group description: -

| | |
|-----------------------|-----------------|
| Reporting group title | treatment group |
|-----------------------|-----------------|

Reporting group description: -

| Serious adverse events | placebo group | treatment group | |
|---|----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 16 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| Non-serious adverse events | placebo group | treatment group | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 6 / 16 (37.50%) | |
| Nervous system disorders | | | |
| Paresthesia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 16 (18.75%) | |
| occurrences (all) | 0 | 3 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 1 / 16 (6.25%) | |
| occurrences (all) | 2 | 1 | |
| abdominal discomfort | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 16 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Constipation | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 14 (28.57%) 4 | 4 / 16 (25.00%) 4 | |
| Respiratory, thoracic and mediastinal disorders respiratory depression subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 16 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported