# Clinical trial results:
# Determination of the minimum local anesthetic dose (MLAD) of spinal chloroprocaine for inguinal herniorrhaphy in ambulatory surgery.

## Summary

| | |
|---|---|
| EudraCT number | 2014-005469-58 |
| Trial protocol | BE |
| Global end of trial date | 24 January 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 July 2020 |
| First version publication date | 15 July 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | AGO/2014/007 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03805503 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Ghent University Hospital |
| Sponsor organisation address | Corneel Heymanslaan 10, Ghent, Belgium, 9000 |
| Public contact | Bimetra Clinics, Ghent University Hospital, +32 93320500, Bimetra.Clinics@uzgent.be |
| Scientific contact | Bimetra Clinics, Ghent University Hospital, +32 93320500, Bimetra.Clinics@uzgent.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 | 15 January 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 24 January 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The primary goal of this study is to determine the minimum effective dose for intrathecal chloroprocaine in inguinal herniorrhaphy in outpatients using a Combined Spinal Epidural (CSE) anesthesia.

Protection of trial subjects:

ethics review and approval, Informed Consent and monitoring

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 16 September 2015 |
| 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: 11 |
| Worldwide total number of subjects | 11 |
| EEA total number of subjects | 11 |

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) | 7 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

From the 16th September 2015 till the 7th September 2017, 12 patients participated in the study. First patient was considered as drop-out. Finally, 11 patients were included in the analysis. All participated patients were male.

### Pre-assignment

Screening details:

- Outpatients for unilateral inguinal hernia repair
- ASA I - II - III

### Period 1

| | |
|---|---|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Chloroprocainehydrochloride |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Chloroprocainehydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Chloroprocainehydrochloride 10mg/ml
Chloroprocainehydrochloride 30mg/ml (rescue medication) in the epidural space
A standard CSE procedure will be conducted. The dura will be punctured using a 27-gauge pencil-point spinal needle and a certain dose of chloroprocaine 1% will be given. After the spinal needle is withdrawn, an epidural catheter will be placed and the epidural needle will be withdrawn.
The first spinal dose of chloroprocaine 1% to start with is 50mg. This dose has been successfully used for spinal anesthesia in hernia repair outpatients to reach an adequate analgesia. Each time there will be added 2,5 microgram of sufentanil for prolongation of the analgesia. The testing interval is 2 mg.

| **Number of subjects in period 1** | Chloroprocainehydrochloride |
|---|---|
| Started | 11 |
| Completed | 11 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | overall trial |

Reporting group description: -

| Reporting group values | overall trial | Total | |
|---|---|---|---|
| Number of subjects | 11 | 11 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 7 | 7 | |
| From 65-84 years | 4 | 4 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 52.5 | | |
| standard deviation | ± 17.12 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 11 | 11 | |
| height<br>Units: cm | | | |
| arithmetic mean | 179.8 | | |
| standard deviation | ± 5.9 | - | |
| weight<br>Units: kg | | | |
| arithmetic mean | 76.9 | | |
| standard deviation | ± 10.67 | - | |

## End points

### End points reporting groups

| Reporting group title | Chloroprocainehydrochloride |
|---|---|

Reporting group description: -

### Primary: Minimum Local Anesthetic Dose (MLAD) of chloroprocaine 1%

| End point title | Minimum Local Anesthetic Dose (MLAD) of chloroprocaine 1%[1] |
|---|---|

End point description:

MLAD of chloroprocaine 1% with 2,5 mcg of sufentanil required for a sensory anesthesia at or above the T6 dermatome at the beginning of surgery with no additional epidural anesthesia required during surgery.
There are four crossovers visible which means that the response in two consecutive patients was four times following an opposite direction and thus successful with the possibility to lower the dose in the next patient. The mean of these doses, belonging to these crossovers is the midpoint estimator and thus the ED50 (95% CI), calculated via the original Dixon and Mood method, was 54 mg (49-54).

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

End point timeframe:

overall study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical ananlyses available

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg | | | | |
| arithmetic mean (confidence interval 95%) | 54 (49 to 54) | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Minimum Local Anesthetic Dose (MLAD) by logistic regression

| End point title | Minimum Local Anesthetic Dose (MLAD) by logistic regression[2] |
|---|---|

End point description:

The second way to determine the ED50 (95% CI) is the logistic regression method which assumes the ED50 value of 55 mg (42-64). The sigmoid dose-response curve illustrates the intersection between a response of 50% and the curve giving the corresponding dose of the ED50.

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

End point timeframe:

overall trial

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical ananlyses available

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg | | | | |
| log mean (confidence interval 95%) | 55 (42 to 64) | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: MLAD determined by PAVA

| End point title | MLAD determined by PAVA[3] |
|---|---|

End point description:

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

End point timeframe:

overall trial

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical ananlyses available

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg | | | | |
| arithmetic mean (confidence interval 95%) | 56 (52 to 58) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: time for regression of two segments

| End point title | time for regression of two segments |
|---|---|

End point description:

Time to two-segment regression varied between 15 en 55 minutes with mean value of 23 min.

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

End point timeframe:

overall study

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 23 (± 13.43) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: ambulation

| End point title | ambulation |
|---|---|

End point description:

Motor recovery lasted from 90 to 177 minutes, depending on whether only spinal or spinal along with epidural analgesia was administered. Ambulation time fluctuated between 160 and 290 minutes

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

End point timeframe:

overall study

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 251.6 (± 71.28) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to micturition

| End point title | Time to micturition |
|---|---|

End point description:

The time of first voiding ranged from 164 to 390 minutes and none of the patients had urinary retention which needed a bladder catheterization.

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

End point timeframe:

Overall trial

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 275.5 (± 70.4) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: time of surgery

| End point title | time of surgery |
|---|---|

End point description:

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

End point timeframe:

overall study

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 42.4 (± 11.06) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: motor recovery

| End point title | motor recovery |
|---|---|

End point description:

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

End point timeframe:

overall trial

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 126 (± 34.7) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Peak block height

| End point title | Peak block height |
|---|---|
| End point description:<br>T1-T10 | |
| End point type | Secondary |
| End point timeframe:<br>overall trial | |

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: mg chloroprocaine 1% | | | | |
| highest sensible block reached T1<br>lowest dermatome at T10 | 54<br>56 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patient satisfaction

| End point title | Patient satisfaction |
|---|---|
| End point description: | |
| End point type | Secondary |
| End point timeframe:<br>overall trial | |

| End point values | Chloroprocaine hydrochloride | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: subjects | | | | |
| satisfied | 2 | | | |
| highly satisfied | 9 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: overall trial | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | CTCAE |
| Dictionary version | 5 |
| **Reporting groups** | |
| Reporting group title | overall trial |

Reporting group description: -

| Serious adverse events | overall trial | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | overall trial | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 11 (81.82%) | | |
| Cardiac disorders | | | |
| Bradycardia | Additional description: Bradycardia (< 50 bpm) has been observed in 7 patients. One patient had a HR below 40 bpm and needed intravenous administration of the drug (i.e. Atropine 0.5 mg). This particular patient had a high sensory block reaching the level of T1 dermatome. | | |
| subjects affected / exposed | 7 / 11 (63.64%) | | |
| occurrences (all) | 7 | | |
| Hypotension | Additional description: The systolic blood pressure in 7 patients and in 3 patients decreased by 20% and 30% respectively the low blood pressure. Similarly, this patient has had the highest sensory block reaching the level of T1 dermatome. | | |
| subjects affected / exposed | 7 / 11 (63.64%) | | |
| occurrences (all) | 7 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 24 January 2018 | It was decided to end the trial because the inclusion was difficult. After 3 years, only 12 patients (including 1 drop-out) were included. The number of patents choosing for a spinal anaesthesia and gives consent to participate into a trial appears to be very small. | - |

Notes:

## Limitations and caveats

None reported