Clinical trial results:

Determination of the minimum local anesthetic dose (MLAD) of spinal chloroprocaine for inguinal herniorrhaphy in ambulatory surgery.

EudraCT number	2014-005469-58	
Trial protocol	BE	
Global end of trial date	24 January 2018	
Result version number	v1 (current)	
This version publication date	15 July 2020	
First version publication date	15 July 2020	

Sponsor protocol code	AGO/2014/007
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03805503
WHO universal trial number (UTN)	-

Notes:

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:

Is trial part of an agreed paediatric investigation plan (PIP)	Νο
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
Notos	

Notes:

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:

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: -

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Actual start date of recruitment	16 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No
NL I	

Notes:

Country: Number of subjects enrolled	Belgium: 11
Worldwide total number of subjects	11
EEA total number of subjects	11
	-

Notes:

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

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.

Screening details:

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

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

	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.

	Chloroprocainehydro chloride
Started	11
Completed	11

Reporting group title	overall trial

Reporting group description: -

	overall trial	Total	
Number of subjects	11	11	
Age categorical			
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			
Units: years			
arithmetic mean	52.5		
standard deviation	± 17.12	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	11	11	
height			
Units: cm			
arithmetic mean	179.8		
standard deviation	± 5.9	-	
weight			
Units: kg			
arithmetic mean	76.9		
standard deviation	± 10.67	-	

Reporting group title	Chloroprocainehydrochloride
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Reporting group description: -

End point titleMinimum Local Anesthetic Dose (MLAD) of chloroprocaine 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

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

No statistical analyses for this end point

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	
NL I	

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 analyses available

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

End point seM

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

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

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

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				

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

End point title	time of surgery
End point description:	
End point type	Secondary
End point timeframe:	
overall study	

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

End point title	motor recovery	
End point description:		
End point type	Secondary	
End point timeframe:		
overall trial		

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

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

	Chloroprocaine hydrochloride		
Subject group type	Reporting group		
Number of subjects analysed	11		
Units: mg chloroprocaine 1%			
highest sensible block reached T1	54		
lowest dermatome at T10	56		

End point title	Patient satisfaction
End point description:	

End point type	Secondary
End point timeframe:	
overall trial	

	Chloroprocaine hydrochloride		
Subject group type	Reporting group		
Number of subjects analysed	11		
Units: subjects			
satisfied	2		
highly satisfied	9		

Timeframe for reporting advers	se events:	
overall trial		
Assessment type	Systematic	
Dictionary name	CTCAE	
Dictionary version	5	
Reporting group title	overall trial	

Reporting group description: -

	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 %

	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)		
Cardiac disorders			
Bradycardia	Additional description: Bra One patient had a HR belo the drug (i.e. Atropine 0.5 reaching the level of T1 de	adycardia (< 50 bpm) has b w 40 bpm and needed intra mg). This particular patient ermatome.	een observed in 7 patients. venous administration of t had a high sensory block
subjects affected / exposed	7 / 11 (63.64%)		
occurrences (all)	7		
Hypotension	Additional description: Th patients decreased by 20% Similarly, this patient has dermatome.	e systolic blood pressure in 6 and 30% respectively the had the highest sensory blo	7 patients and in 3 low blood pressure. ck reaching the level of T1
subjects affected / exposed	7 / 11 (63.64%)		
occurrences (all)	7		

Were there any global interruptions to the trial? Yes

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:

None reported