Clinical trial results:
Randomized, double-blind, prospective, placebo-controlled trial of the effect of intravenous lidocaine infusion for postoperative pain management and bowel function in robot assisted laparoscopic colon surgery.

Summary

EudraCT number	2014-003466-25
Trial protocol	DK
Global end of trial date	31 May 2018

Results information

Result version number	v1 (current)
This version publication date	13 July 2018
First version publication date	13 July 2018
Summary attachment (see zip file)	Randomized, double-blind, prospective, placebo-controlled trial of the effect of intravenous lidocaine infusion for postoperative pain management and bowel function in robot assisted laparoscopic colo (Abstract.docx)

Trial information

Trial identification

Sponsor protocol code	13.024

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Anders Gadegaard Jensen,Anesthesia and Intensive Care Unit, Odense University Hospital
Sponsor organisation address	Søndre Boulevard 29, odense, Denmark, 5000
Public contact	Jan Herzog, Jan Herzog,Anesthesia and Intensive Care Unit, Odense University Hospital, 0045 60709164, anders.gadegaard.jensen@rsyd.dk
Scientific contact	Jan Herzog, Jan Herzog,Anesthesia and Intensive Care Unit, Odense University Hospital, 0045 60709164, anders.gadegaard.jensen@rsyd.dk
Sponsor organisation name	Anders Gadegaard Jensen,Anesthesia and Intensive Care Unit, Odense University Hospital
Sponsor organisation address	Søndre Boulevard 29, Odense C, Denmark, 5000
Public contact	Anders Gadegaard Jensen, Anesthesia and Intensive Care Unit, Odense University Hospital,OUH., Anders Gadegaard Jensen, Anesthesia and Intensive Care Unit, Odense University Hospital,OUH., 0045 65413758, anders.gadegaard.jensen@rsyd.dk
Scientific contact	Anders Gadegaard Jensen, Anesthesia and Intensive Care Unit, Odense University Hospital,OUH., Anders Gadegaard Jensen,

Anesthesia and Intensive Care Unit, Odense University Hospital,OUH., 0045 65413758, anders.gadegaard.jensen@rsyd.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	25 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2017
Global end of trial reached?	Yes
Global end of trial date	31 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the trial is to investigate whether intravenous lidocaine administered perioperatively can significantly reduce postoperative morphine consumption during the first 24 hours postoperatively by robot-assisted laparoscopic colon rectal cancer surgery.

Protection of trial subjects:

The trial participant is carefully observed during the per- and postoperative course with regard to adverse events and events both in the operating room by the anesthetic staff and in the recovery section by the staff here. If any adverse event were observed in this period, they were recorded.Procedures for recording and reporting events / adverse events:
Definitions of events and side effects were divided into the following:
Event: Any unwanted incident in a clinical trial after a drug with a patient or a subject without the need for a correlation between this and the unwanted event.
Adverse Drug Reaction (ADR): Any adverse and undesired reaction to a trial drug regardless of dose.
Unexpected adverse reaction: A side effect, whose grade or seriousness does not match the product information (product summary).
Severe Incidence (SAE) or serious adverse event (SAR): An event or adverse event irrespective of dose results in death, is life threatening, causes hospitalization or prolonged hospitalization, resulting in significant or sustained disability or incapacity or leads to congenital anomaly or malformation.
Unexpected and suspected serious side effects (SUSAR): suspected adverse reactions that are both unexpected and severe.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	10
From 65 to 84 years	40
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

We included adult, Danish speaking patients scheduled for elective robot-assisted laparoscopic colorectal surgery. Exclusion criteria were: allergy for amide localanalgetics, atrioventricular blocks, hepatic-(ALAT, ASAT or bilirubin > 2,5 x upper limit), or renal failure (calculated CrCl<60ml/min), chronic use of opioids or NSAID'S, pregnant or la

Pre-assignment

Screening details:

We included adult, Danish speaking patients scheduled for elective robot-assisted laparoscopic colorectal surgery. Exclusion criteria were: allergy for amide localanalgetics, atrioventricular blocks, hepatic-(ALAT, ASAT or bilirubin > 2,5 x upper limit), or renal failure (calculated CrCl<60ml/min), chronic use of opioids or NSAID'S, pregnant or la

Period 1

Period 1 title	Randomized, double-blind, prospective, p (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline.

Arm type	Experimental
Investigational medicinal product name	lidocaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Before anesthesia induction we gave an equal volume of blinded study medication according to 1,5mg/kg bolus from a solution of 0,5% lidocaine with a rate of 300ml/h. Thereafter we started the continuing infusion of the same volume per hour throughout the surgery ending in the PACU 2 hours after end of surgery. A 70kg patient would get 21ml study medication (either isotonic saline or 0,5% lidocaine) as a bolus and 21ml/h until 2 hours after end of surgery.

Arm title	placebo

Arm description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline

Arm type	Placebo
Investigational medicinal product name	hypotonic saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Before anesthesia induction we gave an equal volume of blinded study medication according to 1,5mg/kg bolus from a solution of 0,5% lidocaine with a rate of 300ml/h. Thereafter we started the continuing infusion of the same volume per hour throughout the surgery ending in the PACU 2 hours after end of surgery. A 70kg patient would get 21ml study medication (either isotonic saline or 0,5% lidocaine) as a bolus and 21ml/h until 2 hours after end of surgery

Number of subjects in period 1	Intervention	placebo
Started	30	30
Completed	30	30

Baseline characteristics

Reporting groups

Reporting group title	Randomized, double-blind, prospective, p

Reporting group description: -

Reporting group values	Randomized, double-blind, prospective, p	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
Adults (18-64 years)	10	10	
From 65-84 years	40	40	
85 years and over	10	10	
Age continuous Units: years			
median	30		
standard deviation	± 30	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	40	40	

Subject analysis sets

Subject analysis set title	We randomized 60 patients in this prospective, randomized, dou
Subject analysis set type	Full analysis

Subject analysis set description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline. The follow up period was 72 hours. Primary outcome was cumulative morphine consumption at 24 hours. Secondary outcomes were cumulative morphine consumption at 72hours, numerical pain score at 24 hours/72hours, length of stay, incidence of use of antiemetics, time until flatus/defecation.

Reporting group values	We randomized 60 patients in this prospective, randomized, dou		
Number of subjects	58		
Age categorical Units: Subjects			
Adults (18-64 years)	10		
From 65-84 years	40		
85 years and over	10		
Age continuous Units: years			
median	29		
standard deviation	± 29		

Gender categorical Units: Subjects			
Female	18		
Male	40		

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline.

Reporting group title	placebo

Reporting group description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline

Subject analysis set title	We randomized 60 patients in this prospective, randomized, dou
Subject analysis set type	Full analysis

Subject analysis set description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline. The follow up period was 72 hours. Primary outcome was cumulative morphine consumption at 24 hours. Secondary outcomes were cumulative morphine consumption at 72hours, numerical pain score at 24 hours/72hours, length of stay, incidence of use of antiemetics, time until flatus/defecation.

Primary: The primary outcome

End point title	The primary outcome

End point description:

End point type	Primary

End point timeframe:

The primary outcome was cumulative morphine consumption at 24hrs after end of surgery.

End point values	Intervention	placebo	We randomized 60 patients in this prospective, randomized, dou	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	58	
Units: cumulative morphine consumption at 24hrs				
number (not applicable)	29	29	58	

Statistical analyses

Statistical analysis title	The primary outcome
Comparison groups	Intervention v placebo

Number of subjects included in analysis	60
Analysis specification	Post-hoc
Analysis type	other[1]
P-value	< 0.05
Method	Regression, Linear

Notes:

[1] - Power calculation was done in advance assuming 30% reduction in morphine consumption (based on prior studies by other groups) in the lidocaine group. We needed a power of 80% to detect a difference defined by a p<0,05. According to this calculation we needed 49 patients and decided to include 60 considering there might be dropouts. The data was analyzed according to the intention-to-treat principle.

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From arriving to the operating theatre until 72 hours after conclusion the surgery.

Assessment type	Systematic

Dictionary used

Dictionary name	GCP
Dictionary version	0

Reporting groups

Reporting group title	Intervention

Reporting group description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline.

Reporting group title	placebo

Reporting group description:

We randomized 60 patients in this prospective, randomized, double blinded trial. The patients were treated with 1,5mg/kg bolus and afterwards 1,5mg/kg/h infusion of lidocaine from before anesthesia induction until 2 hours after end of surgery. The control group received an equal volume of isotonic saline

Serious adverse events	Intervention	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (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: 0 %

Non-serious adverse events	Intervention	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: We did not register any non-serious adverse event in the intervention group.

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