Clinical trial results:
Transversus abdominis plane blok, continous systemic administration of lidocain and patient controlled intravenous morphine - 3 methods for postoperative pain control after laparoscopic colorectal surgery: a randomised comparative trial.

Summary

EudraCT number	2014-001499-73
Trial protocol	BE
Global end of trial date	16 January 2017

Results information

Result version number	v1 (current)
This version publication date	01 January 2020
First version publication date	01 January 2020

Trial information

Trial identification

Sponsor protocol code	GDW04/2014Amendment1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Univeristy Hospitals Leuven
Sponsor organisation address	herestraat, leuven, Belgium,
Public contact	Anesthesie Research, Univeristy Hospitals Leuven, +32 16344620, christel.huygens@uzleuven.be
Scientific contact	Anesthesie Research, Univeristy Hospitals Leuven, +32 16344620, christel.huygens@uzleuven.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	17 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2017
Global end of trial reached?	Yes
Global end of trial date	16 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does a TAP-block offers superior analgesia in comparison with systemic administation of linisol after laparoscopic colo-rectal surgery.

Protection of trial subjects:

To prevent patient discomfort and distress, adequate follow-up and treatment was described in the protocol.
"Postoperative pain in the PACU and on the ward was treated with acetaminophen (15 mg/kg 4/day) and ketorolac (0.5mg/kg 3/day) using a fixed scheme. In addition, each patient received patient-controlled intravenous analgesia (PCIA) with morphine. If the postoperative numeric rating scale (NRS) for pain exceeded 3, an additional bolus of 1 mg of morphine (IV) was given on the PACU. If pain treatment was still insufficient, a clonidine bolus (1µg/kg) was given. PONV prophylaxis was performed with IV dexamethasone and IV ondansetron. PONV rescue treatment consisted of IV-droperidol (PACU) or IV-ondansetron (on the ward)."

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 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: 125
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	87
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

between December 2014 and January 2017

Pre-assignment

Screening details:

125 patients undergoing laparoscopic colorectal surgery were included in this randomized, double-blind controlled clinical trial, patients were randomly allocated to either the quadratus lumborum group (QL-group)(n=50), the lidocaine group (L-group)(n=50) or the placebo group (P-group)(n=25)

Pre-assignment period milestones

Number of subjects started	125
Number of subjects completed	125

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

Blinding implementation details:

To attain blinding of the patients and the investigators, patients in the QL-group and the P-group received a perioperative placebo infusion with saline at the same rate as the lidocaine infusion in the L-group. Moreover, the patients of both the L-group and the P-group received also a QL-block with saline.

Arms

Are arms mutually exclusive?	Yes
Arm title	QL-group

Arm description:

Quadratus lumborum group: patients received TAP-block with ropivacaine 0.25% and clonidine 0.5µg/kg

Arm type	Experimental
Investigational medicinal product name	Ropivacain
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Perineural use

Dosage and administration details:

In patients of the QL-group, a bilateral single shot QL-block was applied under ultrasound guidance before induction of anesthesia. At each side, 30 mL (in patients weighing > 55 kg) or 20 mL (in patients weighing < 55 kg) of ropivacaine 0.25% and clonidine 0.5 µg kg-1 were injected using a 22G needle of 50mm length.

Arm title	L-group

Arm description:

Lidocaine group: patients received infusion with lidocaine 1.5 mg/kg (TAP block with placebo)

Arm type	Experimental
Investigational medicinal product name	Lidocain
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients in the L-group received an intravenous (IV) bolus injection of lidocaine 1.5 mg kg 1 at induction of anesthesia followed by a continuous infusion of 1.5 mg kg-1h-1 which was continued until 4h after arrival at the postoperative anesthesia care unit (PACU).

Arm title	Control

Arm description:

Placebo group, Control group: Saline was given in TAP block, Saline was given in infusion. Only PCIA with morphine (as in QL-group and L-group).

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Perineural use, Intravenous use

Dosage and administration details:

To attain blinding of the patients and the investigators, patients in the QL-group and the P-group received a perioperative placebo infusion with saline at the same rate as the lidocaine infusion in the L-group. Moreover, the patients of both the L-group and the P-group received also a QL-block with saline.

Number of subjects in period 1	QL-group	L-group	Control
Started	50	50	25
Completed	50	50	25

Baseline characteristics

Reporting groups	
Reporting group title	QL-group
Reporting group description:	
Quadratus lumborum group: patients received TAP-block with ropivacaine 0.25% and clonidine 0.5µg/kg	
Reporting group title	L-group
Reporting group description:	
Lidocaine group: patients received infusion with lidocaine 1.5 mg/kg (TAP block with placebo)	
Reporting group title	Control
Reporting group description:	
Placebo group, Control group: Saline was given in TAP block, Saline was given in infusion. Only PCIA with morphine (as in QL-group and L-group).	

Reporting group values	QL-group	L-group	Control
Number of subjects	50	50	25
Age categorical			
age between 18 and 75 years Quadratus lumborum (n=50) 56 (48; 65) years lidocaine : (n=50) 60 (49; 68) years Placebo : (n=25) 62 (59;68) years			
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	59	60	62
inter-quartile range (Q1-Q3)	47.75 to 64.75	48 to 67.75	59 to 68
Gender categorical Units: Subjects			
Female	18	23	11
Male	32	27	14
ASA			
ASA classification			
Units: Subjects			
ASA 1	8	9	7
ASA 2	34	30	14
ASA 3	8	11	4

Weight			
Units: kilogram(s)			
median	80	75	72
inter-quartile range (Q1-Q3)	69 to 90	64 to 81	67 to 86
BMI			
Units: kilogram(s)/square meter			
median	26.4	25	25.4
inter-quartile range (Q1-Q3)	23.9 to 29.4	23 to 27.2	24.2 to 28.4
Height			
Units: cm			
median	171	170	169
inter-quartile range (Q1-Q3)	168 to 180	165 to 178	165 to 175

Reporting group values	Total		
Number of subjects	125		
Age categorical			
age between 18 and 75 years Quadratus lumborum (n=50) 56 (48; 65) years lidocaine : (n=50) 60 (49; 68) years Placebo : (n=25) 62 (59;68) years			
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			
inter-quartile range (Q1-Q3)	-		
Gender categorical			
Units: Subjects			
Female	52		
Male	73		
ASA			
ASA classification			
Units: Subjects			
ASA 1	24		
ASA 2	78		
ASA 3	23		
Weight			
Units: kilogram(s)			
median			
inter-quartile range (Q1-Q3)	-		
BMI			

Units: kilogram(s)/square meter median inter-quartile range (Q1-Q3)	- 		
Height Units: cm median inter-quartile range (Q1-Q3)	- 		

End points

End points reporting groups

Reporting group title	QL-group
Reporting group description:	
Quadratus lumborum group: patients received TAP-block with ropivacaine 0.25% and clonidine 0.5µg/kg	
Reporting group title	L-group
Reporting group description:	
Lidocaine group: patients received infusion with lidocaine 1.5 mg/kg (TAP block with placebo)	
Reporting group title	Control
Reporting group description:	
Placebo group, Control group: Saline was given in TAP block, Saline was given in infusion. Only PCIA with morphine (as in QL-group and L-group).	

Primary: Cumulative morphine usage

End point title	Cumulative morphine usage
End point description:	

End point type	Primary
End point timeframe:	
24 hours after surgery	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: milligram(s)				
arithmetic mean (standard deviation)	37.5 (± 28.4)	40.2 (± 25)	21.8 (± 17)	

Statistical analyses

Statistical analysis title	Cumulative morphine consumption
Statistical analysis description:	
Cumulative morphine consumption the first 24 hours postoperatively	
Comparison groups	QL-group v L-group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.15
Method	t-test, 2-sided

Secondary: Recovery of bowel movement

End point title	Recovery of bowel movement
End point description: Time until defecation	
End point type	Secondary
End point timeframe: Day of discharge (chart review)	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: day				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	3 (2 to 4)	3 (2 to 5)	

Statistical analyses

Statistical analysis title	Time until defecation
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.84
Method	Wilcoxon (Mann-Whitney)

Secondary: Incidence of postoperative nausea and vomiting

End point title	Incidence of postoperative nausea and vomiting
End point description: Incidence of PONV during first 24 hours postoperatively	
End point type	Secondary
End point timeframe: 24 hours after surgery	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: number				
PONV: yes	30	35	16	
PONV: No	20	15	9	

Statistical analyses

Statistical analysis title	incidence of PONV
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.578
Method	Fisher exact

Secondary: Lenght of hospital stay

End point title	Lenght of hospital stay
End point description:	
End point type	Secondary
End point timeframe:	
Day of discharge	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: day				
median (inter-quartile range (Q1-Q3))	4 (3 to 5)	4 (4 to 5)	4 (3 to 5)	

Statistical analyses

Statistical analysis title	Length of hospital stay
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73
Method	Wilcoxon (Mann-Whitney)

Secondary: Clavien-Dindo Classification	
End point title	Clavien-Dindo Classification
End point description: Inhospital morbidity with the Clavien Dindo classification	
End point type	Secondary
End point timeframe: Day of discharge	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: unit(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 0.75)	0 (0 to 1)	

Statistical analyses

Statistical analysis title	Clavien Dindo classification
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.908
Method	Wilcoxon (Mann-Whitney)

Secondary: Cytokine IL-6 day 1	
End point title	Cytokine IL-6 day 1
End point description:	
End point type	Secondary
End point timeframe: Day 1 after surgery	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	15 (7 to 37)	19 (11 to 39)	36 (5 to 72)	

Statistical analyses

Statistical analysis title	Cytokine IL-6 Day 1
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.52
Method	Wilcoxon (Mann-Whitney)

Secondary: CRP	
End point title	CRP
End point description: C-reactive protein as inflammatory parameter at postoperative day 1	
End point type	Secondary
End point timeframe: Day 1 after surgery	

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: milligram(s)/millilitre				
median (inter-quartile range (Q1-Q3))	35 (17 to 55)	42 (23 to 68)	27 (19 to 50)	

Statistical analyses

Statistical analysis title	CRP day 1
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.31
Method	Wilcoxon (Mann-Whitney)

Secondary: Total number of morphine boli

End point title	Total number of morphine boli

End point description:

End point type	Secondary

End point timeframe:

At removal of PCIA system

End point values	QL-group	L-group	Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	25	
Units: unit(s)				
median (inter-quartile range (Q1-Q3))				
Delivered	20 (13 to 31)	22 (13 to 32)	11 (5 to 22)	
Demanded	23 (14 to 38)	28 (14 to 49)	12 (6 to 35)	

Statistical analyses

Statistical analysis title	Delivered morphine boli
Comparison groups	QL-group v L-group v Control
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Start: Enrollment Stop: Until hospital discharge	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	QL-group
Reporting group description: Quadratus lumborum group: patients received TAP-block with ropivacaine 0.25% and clonidine 0.5µg/kg	
Reporting group title	L-group
Reporting group description: Lidocaine group: patients received infusion with lidocaine 1.5 mg/kg (TAP block with placebo)	
Reporting group title	Control
Reporting group description: Placebo group, Control group: Saline was given in TAP block, Saline was given in infusion. Only PCIA with morphine (as in QL-group and L-group).	

Serious adverse events	QL-group	L-group	Control
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 50 (10.00%)	7 / 50 (14.00%)	4 / 25 (16.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Peritonitis			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	QL-group	L-group	Control
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 50 (28.00%)	2 / 50 (4.00%)	6 / 25 (24.00%)
Cardiac disorders			
Arrhythmia	Additional description: Arrythmia as LAST (local anaesthetic systemic toxicity)		
subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	2	2
Nervous system disorders			
Metallic taste	Additional description: Metallic taste as symptom of LAST (local anaesthetic systemic toxicity)		
subjects affected / exposed	9 / 50 (18.00%)	1 / 50 (2.00%)	0 / 25 (0.00%)
occurrences (all)	9	1	0
Ear and labyrinth disorders			
Tinnitus	Additional description: LAST (local anaesthetic systemic toxicity)		
subjects affected / exposed	3 / 50 (6.00%)	1 / 50 (2.00%)	1 / 25 (4.00%)
occurrences (all)	5	5	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2014	1) Quadratus lumborum approach for TAP block 2) Time of TAP block at induction 3) Dosage of local anaesthetics 4) Timepoint blood sample 5) Serum ropivacain and lidocain measurement
20 January 2015	TAP block placement at induction with all patients (for the L-group and control, saline will be used)
22 December 2015	Lidocain determination on tissue that was isolated during surgery.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30004914