



Clinical trial results:

A placebo controlled randomised trial of intravenous lidocaine in accelerating gastrointestinal recovery after colorectal surgery

Summary

EudraCT number	2017-003835-12
Trial protocol	GB
Global end of trial date	10 August 2023

Results information

Result version number	v1 (current)
This version publication date	02 February 2025
First version publication date	02 February 2025

Trial information

Trial identification

Sponsor protocol code	AC17067
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Edinburgh & NHS Lothian
Sponsor organisation address	47 Little France Crescent, Edinburgh , United Kingdom, EH16 4TJ
Public contact	Seonaidh Cotton, The University of Aberdeen, s.c.cotton@abdn.ac.uk
Scientific contact	Thenmalar Vadiveloo, The University of Aberdeen, thenmalar.vadiveloo@abdn.ac.uk

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	18 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 April 2023
Global end of trial reached?	Yes
Global end of trial date	10 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim is an effectiveness analysis to measure whether intravenous lidocaine (given at time of surgery) achieves faster return of gut function for more patients after colorectal surgery. The primary outcome will be the proportion of randomised subjects compared between IV lidocaine and placebo that have achieved return of gut function at 72 hours after their surgery. This will be measured by 'GI-3 recovery' -an endpoint defined as achievement of both of the following two events: tolerating diet (defined as ingestion of food and drink without significant nausea or vomiting for 3 consecutive meals) and passage of flatus OR stool (whichever comes first).

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator:

The comparator is a placebo, which is a 0.9% sterile Sodium Chloride solution for injection. It is a clear and colourless solution. The placebo will appear identical to the IMP.

Actual start date of recruitment	14 August 2018
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	United Kingdom: 557
Worldwide total number of subjects	557
EEA total number of subjects	0

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)	238

From 65 to 84 years	303
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

Participants were identified by site study teams and a member of the usual care team approached patients about study participation at existing points of contact prior to surgery. Patients who wished to participate provided written, informed consent. Participants were recruited between 14th August 2018 and 11th April 2023.

Pre-assignment

Screening details:

In total, 1145 patients were identified/screened, 539 were excluded, 16 patients were recruited to the open study and 590 were consented and randomly assigned to the main study. There were 33 post-randomisation exclusions.

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, Assessor

Blinding implementation details:

Participants, medical staff and study staff/outcome assessors were all blinded in this study. Both study drug and placebo were clear colourless liquids and were packaged in identical containers. Upon randomisation the participant was allocated a unique participant study number and assigned a numbered participant pack. Randomisation triggered a notification email to pharmacy.

Arms

Are arms mutually exclusive?	Yes
Arm title	IV Lidocaine

Arm description:

Sterile solution of Lidocaine 2% made isotonic with Sodium Chloride

Arm type	Experimental
Investigational medicinal product name	IV Lidocaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

The patient received an intravenous bolus of study drug at induction of anaesthesia (1.5mg/kg ideal body weight) given over 20 minutes followed by intravenous infusion of 1.5 mg/hour/kg ideal body weight with a maximum rate of 120mg/hour (6ml/hour) for a minimum of 6 hours up to a maximum of 12 hours. Calculation of the correct infusion rate and administration of the study drug/placebo was undertaken by the responsible anaesthetist for the operation. Exemplar dose calculation tables were provided in the study protocol. Ideal body weight was used rather than actual body weight to prevent the possibility of toxicity by exceeding the upper therapeutic threshold of lidocaine in very overweight patients.

Arm title	Placebo
Arm description:	
0.9% sterile Sodium Chloride solution for injection.	
Arm type	Placebo

Investigational medicinal product name	IV Lidocaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

The patient received an intravenous bolus of study drug at induction of anaesthesia (1.5mg/kg ideal body weight) given over 20 minutes followed by intravenous infusion of 1.5 mg/hour/kg ideal body weight with a maximum rate of 120mg/hour (6ml/hour) for a minimum of 6 hours up to a maximum of 12 hours. Calculation of the correct infusion rate and administration of the study drug/placebo was undertaken by the responsible anaesthetist for the operation. Exemplar dose calculation tables were provided in the study protocol. Ideal body weight was used rather than actual body weight to prevent the possibility of toxicity by exceeding the upper therapeutic threshold of lidocaine in very overweight patients.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion same as IV lidoacaine arm

Number of subjects in period 1	IV Lidocaine	Placebo
Started	279	278
Completed	279	278

Baseline characteristics

Reporting groups

Reporting group title	IV Lidocaine
Reporting group description:	
Sterile solution of Lidocaine 2% made isotonic with Sodium Chloride	
Reporting group title	Placebo
Reporting group description:	
0.9% sterile Sodium Chloride solution for injection.	

Reporting group values	IV Lidocaine	Placebo	Total
Number of subjects	279	278	557
Age categorical			
Age was collected at baseline and reported as n(%) for each category			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (50-74 years)	198	198	396
Adults (18-49 years)	18	19	37
Adults (75 and above)	63	61	124
Age continuous			
Units: years			
arithmetic mean	65.9	66.5	
standard deviation	± 11.0	± 10.7	-
Gender categorical			
Units: Subjects			
Female	122	127	249
Male	157	151	308
Current smoking status			
Units: Subjects			
Yes	24	26	50
No	255	251	506
Missing	0	1	1
BMI			
Units: kg/m2			
arithmetic mean	28.0	28.0	
standard deviation	± 5.6	± 5.4	-
EQ-5D-5L			
Total score for EQ-5D-5L			
Units: Score			

arithmetic mean	0.833	0.825	
standard deviation	± 0.146	± 0.168	-
EQ-5D-5L - Visual analogue scale			
Units: Score			
arithmetic mean	77.7	78.1	
standard deviation	± 18.3	± 18.1	-
Overall Benefit of Analgesia Score			
Units: Score			
arithmetic mean	2.62	2.53	
standard deviation	± 2.87	± 2.69	-
Quality of recovery-15			
Units: Score			
arithmetic mean	96.67	96.11	
standard deviation	± 11.09	± 12.15	-

End points

End points reporting groups

Reporting group title	IV Lidocaine
Reporting group description: Sterile solution of Lidocaine 2% made isotonic with Sodium Chloride	
Reporting group title	Placebo
Reporting group description: 0.9% sterile Sodium Chloride solution for injection.	

Primary: Proportion of randomised subjects that have achieved return of gut function at 72 hours postoperatively

End point title	Proportion of randomised subjects that have achieved return of gut function at 72 hours postoperatively
End point description: Return of gut function was measured by 'GI-3' - composite endpoint defined as achievement of both of the following two events: tolerating diet (defined as ingestion of food and drink without significant nausea or vomiting for 3 consecutive meals) and passage of flatus OR stool (whichever comes first).	
End point type	Primary
End point timeframe: 72 hours post-operative	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Achieved GI-3	160	164		
Did not achieve GI-3	119	114		

Statistical analyses

Statistical analysis title	Generalised linear model
Statistical analysis description: The primary outcome was analysed using a generalised linear model with a logit link function adjusted for the minimisation factors using fixed effects for gender (male, female), age group (<50 years, 50-74 years, 75 years and older), and a random effect for centre.	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.542
Method	Generalised linear model
Parameter estimate	Relative risk
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.07

Secondary: Time to GI-3 recovery

End point title	Time to GI-3 recovery
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total	275	275		

Attachments (see zip file)	Figure1.jpg
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Statistical analyses

Statistical analysis title	Cox-regression model
Statistical analysis description:	
Cox regression adjusted for the minimisation variables; gender, age and centre (the latter via a random effect).	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.17

Secondary: Time to return of gut function using the GI-2 recovery

End point title	Time to return of gut function using the GI-2 recovery
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End point description:

End point type	Secondary
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End point timeframe:

90 days

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total	261	256		

Attachments (see zip file)	Figure 2.jpg
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Statistical analyses

Statistical analysis title	Cox-regression model
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Statistical analysis description:

Cox regression adjusted for the minimisation variables; gender, age and centre (the latter via a random effect).

Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.76
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.23

Secondary: Prolonged Postoperative Ileus

End point title	Prolonged Postoperative Ileus
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End point description:

Proportion of patients who failed to establish GI-3 by 120 hours after surgery.

End point type	Secondary
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End point timeframe:

120 hours post-operative

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
PPOI	44	39		

Statistical analyses

Statistical analysis title	Generalised linear model
Statistical analysis description:	
Generalised linear model with a logit link function adjusted for the minimisation variables; gender, age and centre (the latter via a random effect).	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.491
Method	Generalised linear model
Parameter estimate	Relative risk
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.61

Secondary: Daily Postoperative Nausea and Vomiting (PONV) score

End point title	Daily Postoperative Nausea and Vomiting (PONV) score
End point description:	
End point type	Secondary
End point timeframe:	
Daily until 72 hours after start of operation	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Post-op Day 1: Clinically important - ≥ 5	7	16		
Post-op Day 2: Clinically important - ≥ 5	5	19		
Post-op Day 3: Clinically important - ≥ 5	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Benefit of Analgesia Score

End point title	Overall Benefit of Analgesia Score
End point description: Overall Benefit of Analgesia Score	
End point type	Secondary
End point timeframe: Daily in-hospital up to and including postoperative day 7	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	241		
Units: Values				
arithmetic mean (standard deviation)	2.19 ($\pm$ 2.55)	1.96 ($\pm$ 2.52)		

Statistical analyses

Statistical analysis title	Linear mixed model
Statistical analysis description: Linear mixed model used to analyse the repeated measures of OBAS outcome adjusted for the minimisation variables; gender, age and centre (the latter via a random effect). Treatment effects at each time were derived from the interaction term for time by treatment.	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	485
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.346
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.278

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.856

Secondary: Total postoperative opioid consumption

End point title	Total postoperative opioid consumption
End point description:	
End point type	Secondary
End point timeframe:	
Up to 24 hours post-op	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	210		
Units: OME mg				
median (inter-quartile range (Q1-Q3))	70.6 (30.0 to 150.0)	45.0 (17.1 to 98.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of recovery score

End point title	Quality of recovery score
End point description:	
Quality of recovery score (15-question patient-reported outcome measure)	
End point type	Secondary
End point timeframe:	
Daily while in hospital up to 7 days; also days 7 and 30 days after date of operation.	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	240		
Units: Score				
arithmetic mean (standard deviation)	93.34 (± 9.64)	92.91 (± 9.43)		

Statistical analyses

Statistical analysis title	Linear mixed model
Statistical analysis description:	
Linear mixed model used to analyse the repeated measures of Quality of recovery outcome adjusted for the minimisation variables; gender, age and centre (the latter via a random effect). Treatment effects at each time were derived from the interaction term for time by treatment.	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.801
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	2.73

Secondary: Quality of life assessment - EQ-5D-5L

End point title	Quality of life assessment - EQ-5D-5L
End point description:	
End point type	Secondary
End point timeframe:	
Daily in hospital up to 7 days, day 7, 30 days and 90 days after date of operation.	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	246		
Units: Score				
arithmetic mean (standard deviation)	0.869 ($\pm$ 0.149)	0.871 ($\pm$ 0.138)		

Statistical analyses

Statistical analysis title	Linear mixed model
Statistical analysis description:	
Linear mixed model for repeated measures adjusted for the minimisation variables; gender, age and centre (the latter via a random effect). Treatment effects at each time were derived from the interaction term for time by treatment.	
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.917
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.038
upper limit	0.034

Secondary: Measurement of specific enhanced recovery guideline variables that have been shown to impact GI recovery

End point title	Measurement of specific enhanced recovery guideline variables that have been shown to impact GI recovery
End point description:	
Adherence was defined from the following criteria: Postoperative nausea prophylaxis prescribed regularly; No nasogastric tube placed at operation; Total IV fluids in first 24 hrs from start of anaesthesia <4litres (any fluid type); Preoperative carbohydrate loading drink given; Day 1 mobilisation target achieved; Food offered day 1; Supplement drinks given on day of surgery; IV fluids discontinued within 48 hours of start of operation; Urinary catheter removed within 48 hours of start of operation; Mobilisation target achieved (out of bed for at least 4 hours day 2). "High" adherence was defined if a patient met 7 or more criteria and "low" adherence defined if a patient met less than 5 criteria.	
End point type	Secondary
End point timeframe:	
End of inpatient admission	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
High	100	91		
Moderate	131	143		
Low	48	44		

Statistical analyses

Secondary: Time to achievement of medical criteria for discharge

End point title	Time to achievement of medical criteria for discharge
End point description: Time (days) to meeting medically-defined hospital discharge criteria (independent hydration/nutrition, adequate analgesia by oral route, independent mobilisation, return of gut function by GI-3 definition, no medical contraindication)	
End point type	Secondary
End point timeframe: End of inpatient admission	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Achieved medical criteria	278	277		

Statistical analyses

Statistical analysis title	Cox-regression model
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.914
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.17

Secondary: Patient-reported assessment of readiness for discharge

End point title	Patient-reported assessment of readiness for discharge
End point description: Time (days) to patient-reported readiness for discharge (must also have achieved medical criteria for discharge as noted above)	
End point type	Secondary
End point timeframe: Assessed daily from day 2 onward	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Patient fit for discharge	278	277		

Statistical analyses

Statistical analysis title	Cox regression model
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.867
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.17

Other pre-specified: Total length of hospital stay

End point title	Total length of hospital stay
End point description:	
End point type	Other pre-specified
End point timeframe:	
Total duration of primary admission and any readmission within 30 days	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	277		
Units: days				
arithmetic mean (standard deviation)	6.0 (± 5.9)	5.8 (± 4.5)		

Statistical analyses

Statistical analysis title	Incidence rate ratio
Comparison groups	IV Lidocaine v Placebo
Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.648
Method	Poisson
Parameter estimate	Incidence rate ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.14

Other pre-specified: 30-days mortality

End point title	30-days mortality
End point description:	
End point type	Other pre-specified
End point timeframe:	
30 days after date of operation.	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Died	1	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 90 days mortality

End point title	90 days mortality
End point description:	
End point type	Other pre-specified
End point timeframe:	
90 days after date of operation	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Died	2	3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Unplanned re-admissions within 90 days of date of operation

End point title	Unplanned re-admissions within 90 days of date of operation
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End point description:

End point type	Other pre-specified
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End point timeframe:

90 days from date of operation

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	277		
Units: Total				
No with unplanned re-admission	31	34		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Unplanned re-admission after discharge, and within 30 days of operation

End point title	Unplanned re-admission after discharge, and within 30 days of operation
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End point description:

End point type	Other pre-specified
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End point timeframe:

30 days from date of operation

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	277		
Units: Total				
No with unplanned re-admission	10	23		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Major complications

End point title	Major complications
End point description:	
End point type	Other pre-specified
End point timeframe:	
Up to 30 days from date of operation	

End point values	IV Lidocaine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	278		
Units: Total				
Complication of Clavien-Dindo grade 3 and above	13	12		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 30 days post-operation

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	IV Lidocaine
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Reporting group description:

Sterile solution of Lidocaine 2% made isotonic with Sodium Chloride

Reporting group title	Placebo
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Reporting group description:

0.9% sterile Sodium Chloride solution for injection.

Serious adverse events	IV Lidocaine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 279 (1.43%)	9 / 278 (3.24%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Procedural haemorrhage, Anastomotic haemorrhage, Gastrointestinal procedural complication,	Additional description: Other term: Postoperative wound complication		
subjects affected / exposed	2 / 279 (0.72%)	3 / 278 (1.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia, Atrial fibrillation			
subjects affected / exposed	0 / 279 (0.00%)	2 / 278 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 279 (0.36%)	2 / 278 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	0 / 279 (0.00%)	2 / 278 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IV Lidocaine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 279 (12.90%)	27 / 278 (9.71%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm recurrence			
subjects affected / exposed	1 / 279 (0.36%)	0 / 278 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Anastomotic leak, Gastrointestinal procedural complication, Postoperative ileus	Additional description: Stoma complications, Toxicity to various agents, Postoperative wound complication, Post procedural haemorrhage		
subjects affected / exposed	24 / 279 (8.60%)	19 / 278 (6.83%)	
occurrences (all)	43	25	
Cardiac disorders			
Bradycardia, Supraventricular tachycardia, Nodal arrhythmia, Atrial fibrillation, Sinus arrhythmia,	Additional description: Tachycardia		
subjects affected / exposed	10 / 279 (3.58%)	4 / 278 (1.44%)	
occurrences (all)	10	4	
Nervous system disorders			

Headache, Cerebrovascular accident, Aphasia, Dizziness subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1	3 / 278 (1.08%) 3	
General disorders and administration site conditions Oedema peripheral, Hyperhidrosis, Adverse drug reaction, Multiple organ dysfunction syndrome subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 2	2 / 278 (0.72%) 3	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 279 (0.00%) 0	1 / 278 (0.36%) 1	
Gastrointestinal disorders Melaena, Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1	1 / 278 (0.36%) 1	
Skin and subcutaneous tissue disorders Pruritus, Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 279 (0.00%) 0	2 / 278 (0.72%) 2	
Psychiatric disorders Psychotic disorder, Confusional state subjects affected / exposed occurrences (all)	1 / 279 (0.36%) 1	3 / 278 (1.08%) 3	
Renal and urinary disorders Urinary retention, Acute kidney injury subjects affected / exposed occurrences (all)	2 / 279 (0.72%) 2	1 / 278 (0.36%) 1	
Infections and infestations Pelvic abscess, Lower respiratory tract infection, Postoperative wound infection, COVID-19 subjects affected / exposed occurrences (all)	Additional description: Abdominal infection, Pneumonia, Influenza, Herpes zoster, Urinary tract infection, Stoma site infection		
	9 / 279 (3.23%) 9	8 / 278 (2.88%) 9	
Metabolism and nutrition disorders Hypokalaemia, Hypophosphataemia			

subjects affected / exposed	1 / 279 (0.36%)	1 / 278 (0.36%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 June 2019	Administrative changes. Clarification of definition of reoperation/major complications. Addition of benign polyps and benign stricture to the inclusion criteria. Change of processes around co-enrolment, recording participants who do not complete questionnaires. Clarification of prohibited medications and adverse event recording (including common events after surgery). Addition of new section on data management (personal data, transfer of data, data controller, data breaches).
08 September 2020	Administrative changes. Removal of exploratory open RCT. Clarification on the use of robotic laparoscopic surgery. Changes to consent procedures, including consent by phone and post to give greater flexibility during COVID.
17 March 2022	Administrative changes. Change to the study duration - following an extension to the recruitment period. Clarification to protocol text - including updates to remove text relating to primary endpoint that is not applicable due to the time frame around the endpoint of 72 hours. Clarification on the recording of post randomisation exclusions. Clarification to emergency unblinding text to add in information about conversions from minimally invasive to open surgeries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	Recruitment to ALLEGRO was paused on 20 March 2020 at the start of the COVID-19 pandemic. The Sponsor agreed to re-open recruitment on 7 July 2020. The essential nature of this type of surgery (predominantly for cancer) meant that eligible cases were presenting during the pandemic. The original design of the study had integrated trial processes into existing surgical patient pathways, therefore no change of trial design was required to mitigate the impact of COVID. However, as noted above, an amendment was approved to permit verbal agreement prior to written informed consent to permit randomisation in advance of admission.	07 July 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

For pragmatic reasons relatively short durations of infusion were delivered in ALLEGRO - we cannot discount the possibility that longer duration might be effective.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39602290>

<http://www.ncbi.nlm.nih.gov/pubmed/35090535>