Clinical trial results:
Individualized Pneumoperitoneum Pressure in Colorectal laparoscopic surgery versus standard therapy (IPPCollapse II)

Summary

EudraCT number	2016-001693-15
Trial protocol	ES
Global end of trial date	19 November 2018

Results information

Result version number	v1 (current)
This version publication date	05 February 2022
First version publication date	05 February 2022
Summary attachment (see zip file)	Results Article (Artículo resultados.pdf) Protocol Article (Artículo protocolo.pdf)

Trial information

Trial identification

Sponsor protocol code	IPPCollapse-II

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Instituto de Investigación Sanitaria La Fe de Valencia
Sponsor organisation address	Avenida Fernando Abril Martorell, Torre 106 A planta 7, Valencia, Spain, 46026
Public contact	Jose María Millan Salvador, Instituto de Investigación Sanitaria La Fe, Instituto de Investigaión Sanitaria La Fe de Valencia, 34 961246611, investigacion_clinica@iislafe.es
Scientific contact	Jose María Millan Salvador, Instituto de Investigación Sanitaria La Fe, Instituto de Investigaión Sanitaria La Fe de Valencia, 34 961246611, investigacion_clinica@iislafe.es

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	19 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the post-operative recovery quality of the Individualized Pneumoperitoneum Pressure Therapy in Colorectal laparoscopic surgery versus standard therapy using a quality validated scale of postoperative recovery (PQRS- Postoperative Quality of Recovery Scale) within 15 minutes (T15) and 40 minutes (T40) of their stay in the Post-Anaesthesia Recovery Unit and the day 1 (POD1) and day 3 (POD3) of the postoperative (POD3 Postoperative Day).

Protection of trial subjects:

The reference study was conducted in Spain under the legal framework of Royal Decree 1090/2015. It has been performed in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the General Assembly of the World Medical Association (1996). In addition, the study has been conducted in accordance with the protocol, good clinical practice (GCP) in accordance with the guidelines of the international conference on harmonization (ICH) and regulatory requirements for participating institutions.

An appropriately performed informed consent has been used, in compliance with GCP according to ICH guidelines and approved by the CEIm of the Hospital Universitario y Politécnico La Fe. Prior to inclusion of subjects in the study, a copy of the CEIm-approved informed consent has been reviewed with the prospective participant, signed and dated. The investigator has provided a copy of each subject's signed informed consent form and has retained a copy in the subject's study file.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2017
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	Spain: 166
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	166
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment started on 01 February 2017, and ended on 16 November 2018. A number of 204 patients were included, 166 patients completed all the study proceadures and 38 patients were excluded.

Pre-assignment

Screening details:

Patients enrolled were more than 18 years old, whose surgery was clasified in ASAI-III following the American Society of Anesthesiologists classification, without cognitive deficit, and with previous informed consent signed.

Pre-assignment period milestones

Number of subjects started	166
Number of subjects completed	166

Period 1

Period 1 title	Experimental proceadure (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Individualized Pneumoperitoneum

Arm description:

Patients allocated in Individualized Pneumoperitoneum

Arm type	Experimental
Investigational medicinal product name	Rocuronium
Investigational medicinal product code	29349900
Other name	Rocuronium Bromide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Induction dose 0.6-1mg/kg and continuous perfussion 0.15-0.6,g/kg/h

Investigational medicinal product name	Bridion
Investigational medicinal product code	08466001
Other name	Sugammadex
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

4mg/kg

Arm title	Standard Pneumoperitoneum

Arm description:

Patients allocated in Standard Pneumoperitoneum

Arm type	Active comparator

Investigational medicinal product name	Non-depolarizing neuromuscular blocking agent
Investigational medicinal product code	
Other name	Rocuronium, cisatracurium, atracurium
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Patients receive moderate neuromuscular blockade with rocuronium, cisatracurium or atracurium throughout surgery to maintain a train of four (TOF) between 2 and 4.

Investigational medicinal product name	Neostigmine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

2.5mg or 30–50 μg·kg− 1 according to usual care

Number of subjects in period 1	Individualized Pneumoperitoneum	Standard Pneumoperitoneum
Started	85	81
Completed	85	81

Baseline characteristics

Reporting groups	
Reporting group title	Individualized Pneumoperitoneum
Reporting group description: Patients allocated in Individualized Pneumoperitoneum	
Reporting group title	Standard Pneumoperitoneum
Reporting group description: Patients allocated in Standard Pneumoperitoneum	

Reporting group values	Individualized Pneumoperitoneum	Standard Pneumoperitoneum	Total
Number of subjects	85	81	166
Age categorical Units: Subjects			
Adults from 58-74 years	68	0	68
Adults from 59-77 years	0	67	67
Adults from 18-58 years	17	14	31
Gender categorical Units: Subjects			
Female	27	36	63
Male	58	45	103

End points

End points reporting groups

Reporting group title	Individualized Pneumoperitoneum
Reporting group description:	
Patients allocated in Individualized Pneumoperitoneum	
Reporting group title	Standard Pneumoperitoneum
Reporting group description:	
Patients allocated in Standard Pneumoperitoneum	

Primary: Physiological Postoperative Quality of Recovery (PQRS)

End point title	Physiological Postoperative Quality of Recovery (PQRS)

End point description:

The Postoperative Quality of Recovery Scale (PQRS), used to assess the primary endpoint, is a verbal survey tool that assesses recovery in five domains: physiological, nociceptive, emotional, functional and cognitive; it also collects data on overall patient perspective15. Each of these domains is assessed by means of multiple items on an ordinal scale and compared with baseline to evaluate recovery. A baseline PQRS score was obtained before surgery. After surgery, the PQRS score was obtained at 15 and 40 min after arrival in the postanaesthesia care unit, and in the ward during the morning of postoperative day (POD) 1 and POD 3. It was anticipated that patients would stay in the hospital of surgery for at least 3 days, based on local experience. If the patient was discharged before day 3, it was planned to censor data from the point of last follow-up within the hospital of surgery.

End point type	Primary

End point timeframe:

At 15 and 40 min after arrival i the postanaesthesia care unit and in the ward during the morning of postperative day 1 (POD1) and POD3

End point values	Individualized Pneumoperitoneum	Standard Pneumoperitoneum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	81		
Units: % of patients recovered				
15 min	38	24		
40 min	73	50		
Day 1	75	73		
Day 3	73	75		

Statistical analyses

Statistical analysis title	Two tailed T Test

Statistical analysis description:

All analyses were undertaken using R software version 3.5.2. Two-tailed P <0050 was considered statistically significant and no correction for multiple comparisons was preplanned.

Comparison groups	Individualized Pneumoperitoneum v Standard

	Pneumoperitoneum
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.19
upper limit	6.4
Variability estimate	Standard error of the mean
Dispersion value	1.82

Secondary: Nociceptive Postoperative Quality of Recovery (PQRS)

End point title	Nociceptive Postoperative Quality of Recovery (PQRS)

End point description:

End point type	Secondary

End point timeframe:

15, 40 minutes after surgery, and at postoperative day 1 and 3.

End point values	Individualized Pneumoperitoneum	Standard Pneumoperitoneum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	81		
Units: % Patients recovered				
15 min	60	49		
40 min	73	47		
Day 1	37	35		
Day 3	58	37		

Statistical analyses

Statistical analysis title	Two tailed T Test
Comparison groups	Standard Pneumoperitoneum v Individualized Pneumoperitoneum

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [1]
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[1] - All analyses were undertaken using R software version 3.5.2. Two-tailed P <0050 was considered statistically significant and no correction for multiple comparisons was preplanned.

Secondary: Emotionall Postoperative Quality of Recovery (PQRS)

End point title	Emotionall Postoperative Quality of Recovery (PQRS)

End point description:

End point type	Secondary

End point timeframe:

PQRS score was obtained at 15 and 40 min after arrival in the postanaesthesia care unit, and in the ward during the morning of postoperative day (POD) 1 and POD 3

End point values	Individualized Pneumoperitoneum	Standard Pneumoperitoneum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	81		
Units: %o of Patients recovered				
15 min	88	75		
40 min	85	75		
Day 1	80	75		
Day 3	77	73		

Statistical analyses

Statistical analysis title	Two tailed T Test

Statistical analysis description:

All analyses were undertaken using R software version 3.5.2. Two-tailed P <0050 was considered statistically significant and no correction for multiple comparisons was preplanned.

Comparison groups	Standard Pneumoperitoneum v Individualized Pneumoperitoneum

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	4.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	15.29
Variability estimate	Standard error of the mean
Dispersion value	1.18

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All events that meet the definition of an AE and occur within the period from the time the patient signs the informed consent form until 28 days after the end of treatment should be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Experimental treatment
Reporting group description: -	
Reporting group title	Control treatment
Reporting group description: -	

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: No data indicated in final report

Serious adverse events	Experimental treatment	Control treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 85 (5.88%)	8 / 81 (9.88%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Surgical and medical procedures			
Anastomotik leak			
subjects affected / exposed	1 / 85 (1.18%)	3 / 81 (3.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Recurrent cardiac decompensation			
subjects affected / exposed	0 / 85 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Wound abscess			
subjects affected / exposed	1 / 85 (1.18%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal wound			

subjects affected / exposed	0 / 85 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gastrointestinal disorders			
Paralytic ileus			
subjects affected / exposed	1 / 85 (1.18%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal Pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemoperitoneum			
subjects affected / exposed	0 / 85 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 85 (1.18%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Experimental treatment	Control treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 85 (0.00%)	0 / 81 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 December 2016	Not specified in Final report

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/32506481

http://www.ncbi.nlm.nih.gov/pubmed/30944044