Clinical trial results:
Erector spinae plane (ESP) block versus intercostal nerve blocks (ICNB) in uniportal videoscopic assisted thoracic surgery (VATS): A multicenter double-blind, prospective, randomized controlled trial.

Summary

EudraCT number	2021-006201-29
Trial protocol	BE
Global end of trial date	23 February 2024

Results information

Result version number	v1 (current)
This version publication date	14 August 2024
First version publication date	14 August 2024

Trial information

Trial identification

Sponsor protocol code	SC102021

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium,
Public contact	Research anesthesie, University Hopitals Leuven, +32 16344270, steve.coppens@uzleuven.be
Scientific contact	Research anesthesie, Anesthesie, +32 16344270, steve.coppens@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	05 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2024
Global end of trial reached?	Yes
Global end of trial date	23 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of the erector spinae block with the intercostal nerve block.

Protection of trial subjects:

All source data will be kept at a secured location with restricted access at all times. These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data protection laws and regulations and more in particular the EU General Data Protection Regulation 2016/679 (GDPR) and relevant national laws implementing the GDPR. Appropriate technical and organizational measures to protect the data against unauthorized disclosure or access, accidental or unlawful destruction, or accidental loss or alteration must be established. Trial staff whose responsibilities require access to personal data agree to keep the data confidential.
The Investigator and the Participating Site(s) (as applicable) shall treat all information and data relating to the Trial disclosed to them as confidential and shall not disclose such information to any third parties or use such information for any purpose other than the objectives of the Trial as described in this protocol. The collection, processing and disclosure of personal data, such as participant health and medical information is subject to compliance with applicable laws and regulations regarding personal data protection and the processing of personal data

Background therapy:

3.7 Concomitant medication (non-IMP)
During the perioperative phase until 24 hours postoperatively, standard multimodal analgesia will consist of paracetamol 15mg/kg IV 4q and metamizole 1000 mg IV 4 q and morphine IV loading dose of 0,1 mg/kg. Patient Controlled Intravenous Analgesia (PCIA) with morphine (lockout 1.5mg every 7 minutes, with a maximum dose of 30mg over 4 hours) will be initiated in the PACU. Co-analgesic drugs that may affect postoperative pain levels such as intravenous lidocaine, gabapentinoids, ketamine, clonidine-hydrochloride and tramadol are not allowed (except in case of rescue treatment, see below).
3.8 Rescue treatment
In case of severe postoperative pain despite adequate use of the morphine PCIA, an extra bolus of morphine can be given IV until adequate pain levels (NRS ≤ 3) are reached (1-2 mg IV up to 0,1-0,2 mg/kg). In case of persistent pain and NRS scores ≥ 6, rescue medication will be initiated. In addition, a bolus of ketamine 0.1 mg/kg IV will be titrated. In case of insufficient effects and a persistent NRS ≥ 6, a bolus of clonidine 1 to 2 µg/kg can be given IV.

Evidence for comparator:

The current lack of evidence surrounding the ESP, warrants further investigation. Furthermore, there is a general calling for well-designed robust multicenter prospective randomized control trials regarding the ESP. (25) Next to the scarcity of evidence some other problems regarding the ESP block concern us. Specific regional anesthesia training and expensive resources are required to perform the block safely. Like all fascial plane blocks, which are volume dependent blocks, systemic toxicity is a real danger. In addition the ESP block requires meticulous timing and adjusting operative schedule if it is pre-emptively placed in an awake patient. A fully equipped block room and staffing is needed. If placed intra-operatively, during general anesthesia, additional time is required to use ultrasound, position the patient and to effectively block using regional anesthesia disposable trays and equipment. We therefor hypothesize that a simple well-known, tried and tested block like the ICNB, easily performed by the surgeon intra-operatively is more cost-effective and superior to the ESP block. Currently, to our knowledge, there is only one active study (single center) comparing ICNB versus ESP block for VATS surgery (Erector Spinae Plane Block Versus Intercostal for VATS - Full Text View - ClinicalTrials.gov).

Actual start date of recruitment	18 April 2022
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: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	60
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From March 2022 to February 2024, 124 patients were assessed for eligibility in both study centers.

Pre-assignment

Screening details:

Eligibility: all patient is scheduled for elective single port video thoracoscopic surgery
age between 18-80 and BMI below 40, ASA I- IV without chronic pain medication or liver and kidney function impairment

Period 1

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

Blinding implementation details:

Patients were randomized using a computer-generated permuted block randomization sequence (variable block size with 1:1 allocation). Enclosing assignments in opaque, sequentially numbered, sealed envelopes ensured allocation concealment. At the end of surgery, the randomization envelope was opened and trial medication was prepared by an independent member of the research team not involved in the study or subject's care. Syringes were labelled as "trial medication", to guarantee blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	ICB active (ESP Placebo)

Arm description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,5%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml saline 0.9% placebo)

Arm type	Active comparator
Investigational medicinal product name	Ropivacaine 0.5% and Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

30 ml ropivacaine and 30 ml saline 0.9%

Investigational medicinal product name	Saline 0.9% and Ropivacaine 0.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

30 ml ropivacaine and 30 ml saline 0.9%

Arm title	ESP active (ICB placebo)

Arm description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,9% saline) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml 0.5% ropivacaine)

Arm type	Active comparator
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

Saline 0.9% 30 ml

Investigational medicinal product name	ropivacaine 0.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infiltration

Dosage and administration details:

ropivacein 0.5% 30 ml

Number of subjects in period 1	ICB active (ESP Placebo)	ESP active (ICB placebo)
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	ICB active (ESP Placebo)

Reporting group description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,5%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml saline 0.9% placebo)

Reporting group title	ESP active (ICB placebo)

Reporting group description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,9% saline) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml 0.5% ropivacaine)

Reporting group values	ICB active (ESP Placebo)	ESP active (ICB placebo)	Total
Number of subjects	50	50	100
Age categorical			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: Subjects			
Adults (18-64 years)	21	26	47
From 65-84 years	29	24	53
Age continuous			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: years			
geometric mean	63.06	64.76	
standard deviation	± 12.33	± 9.052	-
Gender categorical			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: Subjects			
Female	24	21	45
Male	26	29	55

ICB active (ESP Placebo) Units: Subjects			
study	50	50	100

study Units: patients			
geometric mean	63.06	64.75	
standard deviation	± 12.33	± 9.052	-

Subject analysis sets

Subject analysis set title	ESP active (ICB Placebo)
Subject analysis set type	Intention-to-treat
Subject analysis set description: morphine consumption and NRS pain scores over 24 hours	
Subject analysis set title	ICB active (ESP Placebo)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Morphine consumption and pain scores NRS over 24 hours	

Reporting group values	ESP active (ICB Placebo)	ICB active (ESP Placebo)	
Number of subjects	50	50	
Age categorical			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: Subjects			
Adults (18-64 years)	21	26	
From 65-84 years	29	24	
Age continuous			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: years			
geometric mean	64.76	63.06	
standard deviation	± 9.052	± 12.33	
Gender categorical			
The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (either 30 ml ropivacaine 0,5% or 30 ml normal saline 0,9%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to			
Units: Subjects			
Female	21	24	
Male	29	26	
ICB active (ESP Placebo) Units: Subjects			
study	50	50	

study			
Units: patients			
geometric mean	64.75	63.06	
standard deviation	± 9.052	± 12.33	

End points

End points reporting groups

Reporting group title	ICB active (ESP Placebo)

Reporting group description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,5%) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml saline 0.9% placebo)

Reporting group title	ESP active (ICB placebo)

Reporting group description:

The intercostal nerve blocks were performed by experienced surgeons at the end of surgery utilizing a small intramuscular needle attached to an intravenous line with syringe mounted on a thoracoscopic clamp. (Fig. 1) They infiltrated 6-7 different intercostal spaces dividing the 30 ml trial medication (30 ml ropivacaine 0,9% saline) over each segment. The erector spinae plane block was placed at the end of surgery in lateral decubitus prior to reversal of anesthesia. A high-frequency 10-13 MHz linear ultrasound transducer (C 60Xi Fujifilm, Bothell USA), connected to a high-resolution ultrasound machine (Sonosite SII, Fujifilm, Bothell USA), was placed at T5-T6 to evaluate the rhomboid and trapezius muscles inceting 30 ml trial medication (30 ml 0.5% ropivacaine)

Subject analysis set title	ESP active (ICB Placebo)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

morphine consumption and NRS pain scores over 24 hours

Subject analysis set title	ICB active (ESP Placebo)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Morphine consumption and pain scores NRS over 24 hours

Primary: Morphine consumption 12 hours

End point title	Morphine consumption 12 hours

End point description:

End point type	Primary

End point timeframe:

Assessed 12 hours post intubation

End point values	ICB active (ESP Placebo)	ESP active (ICB placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: mg				
median (inter-quartile range (Q1-Q3))	9 (3 to 15)	15 (10.5 to 24.5)		

Statistical analyses

Statistical analysis title	Primary Outcome
Comparison groups	ICB active (ESP Placebo) v ESP active (ICB placebo)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided
Variability estimate	Standard deviation

Secondary: Morphine consumption 24 hours	
End point title	Morphine consumption 24 hours
End point description:	
End point type	Secondary
End point timeframe:	
Assessed 24 hours after extubation	

End point values	ICB active (ESP Placebo)	ESP active (ICB placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: mg				
median (inter-quartile range (Q1-Q3))	15 (6 to 23)	19.75 (12 to 39)		

Statistical analyses

Statistical analysis title	Key Secondary outcome
Comparison groups	ICB active (ESP Placebo) v ESP active (ICB placebo)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From enrollment until 24 after extubation

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Active ICB (ESP Placebo)
Reporting group description: -	
Reporting group title	Active ESP (ICB Placebo)

Reporting group description: -

Serious adverse events	Active ICB (ESP Placebo)	Active ESP (ICB Placebo)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 50 (12.00%)	4 / 50 (8.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
De novo atrial fibrillation			
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged air leak	Additional description: sometimes needing new thoracic drain		
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Active ICB (ESP Placebo)	Active ESP (ICB Placebo)	
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 50 (18.00%)	14 / 50 (28.00%)	
Gastrointestinal disorders PONV subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 23	14 / 50 (28.00%) 23	

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