Clinical trial results:
Multicentric, comparative, randomized, open study comparing an early post-operative prophylactic non-invasive ventilation (NIV) to standard post-operative care in patients at high-risk of respiratory complications according to ARISCAT preoperative scoring system whose surgery is performed under general or loco-regional anesthesia (ANTICIPUSC).

Summary

EudraCT number	2017-001011-36
Trial protocol	FR
Global end of trial date	16 October 2019

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	ICO-A-2016-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03629431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	INSTITUT DE CANCEROLOGIE DE L'OUEST
Sponsor organisation address	INSTITUT DE CANCEROLOGIE DE L'OUEST 15 R ANDRE BOCQUEL 49055 ANGERS CEDEX 02, ANGERS 02, France, 49055
Public contact	DRCI , INSTITUT DE CANCEROLOGIE DE L'OUEST, 33 240 67 97 47, promotionrc@ico.unicancer.fr
Scientific contact	DRCI , INSTITUT DE CANCEROLOGIE DE L'OUEST, 0241352700 240 67 97 47, promotionrc@ico.unicancer.fr

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	23 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 October 2019
Global end of trial reached?	Yes
Global end of trial date	16 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of a preventive non-invasive ventilation to standard care
On the incidence of postoperative pulmonary complications of acute respiratory failure type, within 7 days post-operative in intra-hospital, in patients at high risk according to ARISCAT scoring system.

Protection of trial subjects:

In order to ensure the protection of the rights and safety of trial subjects, this clinical trial was performed in compliance with the principles laid down in the declaration of Helsinki, good clinical practice and European regulation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2017
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	France: 253
Worldwide total number of subjects	253
EEA total number of subjects	253

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)	226

From 65 to 84 years	25
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients eligible for the study will be seen in screening's visit to check the inclusion and exclusion criteria.
1149 patients assessed for eligibility

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm experimental : prophylactic NIV

Arm description:

In the intervention treatment arm, all patients were transferred to an intermediate or intensive care unit in order to receive noninvasive ventilation as soon as possible after estuation

Arm type	Experimental
Investigational medicinal product name	Oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gas for dispersion for infusion
Routes of administration	Inhalation use

Dosage and administration details:

Noninvasive ventilation was started with an inspiratory pressure support of 5 to 8 cmH2O, and the level was increased progressively by 2 to 3 cmH2O until respiratory comfort was obtained with a tidal volume of 6 to 8 mL/kg of predicted body weight 27 and a respiratory rate lower than 30/min. Positive end-expiratory pressure (PEEP) was started at 5 cmH2O and increased as needed to a maximum of 10 cm H2O. The fraction of inspired oxygen (FiO2) and PEEP were titrated to obtain a SpO2 of > 92% or a PaO2 of > 70 mmHg. Total airway pressure (PEEP + inspiratory pressure support) was maintained at less than 20 cmH2O to avoid gastric distention or anastomotic leakage 19

Arm title	Arm control : standard care

Arm description:

All patients received therapeutic measures necessary for optimal care, including perioperative analgesia, chest physiotherapy, and bronchodilator administration as needed.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Arm experimental : prophylactic NIV	Arm control : standard care
Started	125	128
Completed	125	128

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	253	253	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	226	226	
From 65-84 years	25	25	
85 years and over	2	2	
Age continuous Units: years			
geometric mean	67.4		
standard deviation	± 10.5	-	
Gender categorical Units: Subjects			
Female	50	50	
Male	203	203	

End points

End points reporting groups

Reporting group title	Arm experimental : prophylactic NIV
Reporting group description:	
In the intervention treatment arm, all patients were transferred to an intermediate or intensive care unit in order to receive noninvasive ventilation as soon as possible after estuation	
Reporting group title	Arm control : standard care
Reporting group description:	
All patients received therapeutic measures necessary for optimal care, including perioperative analgesia, chest physiotherapy, and bronchodilator administration as needed.	

Primary: Acute respiratory failure within the first 7 days following surgery

End point title	Acute respiratory failure within the first 7 days following surgery
End point description:	
End point type	Primary
End point timeframe:	
7 days	

End point values	Arm experimental : prophylactic NIV	Arm control : standard care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	128		
Units: patients	30	35		

Statistical analyses

Statistical analysis title	Efficacy results
Comparison groups	Arm experimental : prophylactic NIV v Arm control : standard care
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.543
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From signing the consentment until 7 days post surgery	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Arm experimental : prophylactic NIV
Reporting group description: -	
Reporting group title	Arm control : standard care
Reporting group description: -	

Serious adverse events	Arm experimental : prophylactic NIV	Arm control : standard care	
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 125 (20.00%)	23 / 128 (17.97%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	3	2	
Injury, poisoning and procedural complications			
Air embolism			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
post procedural cardiogenic shock			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	4 / 125 (3.20%)	3 / 128 (2.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural stroke			

subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 125 (0.80%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pericardial effusion			
subjects affected / exposed	1 / 125 (0.80%)	3 / 128 (2.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			

subjects affected / exposed	0 / 125 (0.00%)	2 / 128 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial haemorrhage			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
necrositing oesophagitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial fistula			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 125 (1.60%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hemothorax			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 125 (1.60%)	2 / 128 (1.56%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Mediastinitis			
subjects affected / exposed	2 / 125 (1.60%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 128 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	0 / 125 (0.00%)	1 / 128 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm experimental : prophylactic NIV	Arm control : standard care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 125 (100.00%)	128 / 128 (100.00%)	

Injury, poisoning and procedural complications			
Postopoperative pulmonary complication			
subjects affected / exposed	125 / 125 (100.00%)	128 / 128 (100.00%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Chirurgical complication			
subjects affected / exposed	7 / 125 (5.60%)	17 / 128 (13.28%)	
occurrences (all)	0	0	
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	67 / 125 (53.60%)	74 / 128 (57.81%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Multiple organ failure			
subjects affected / exposed	37 / 125 (29.60%)	52 / 128 (40.63%)	
occurrences (all)	0	0	
Complications of non invasive ventilation			
subjects affected / exposed	69 / 125 (55.20%)	33 / 128 (25.78%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Digestive disorders			
subjects affected / exposed	58 / 125 (46.40%)	55 / 128 (42.97%)	
occurrences (all)	0	0	
Psychiatric disorders			
psychiatric disorders			
subjects affected / exposed	28 / 125 (22.40%)	26 / 128 (20.31%)	
occurrences (all)	0	0	
Infections and infestations			
Infection			
subjects affected / exposed	37 / 125 (29.60%)	55 / 128 (42.97%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2018	- Updated withdrawal of patient definition
04 March 2019	- Change the organization of DSMB - Update to the list of investigator(s) - Extend the period of inclusions - Update of pharmacovigilance contact details - Update the regulatory references relating to the General Data Protection Regulations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported