Clinical trial results:
Evaluation of REMIFENTANIL as an alternative to curare for rapid sequence anesthetic induction in patients at risk of gastric fluid inhalation

Summary

EudraCT number	2019-000753-31
Trial protocol	FR
Global end of trial date	22 April 2021

Results information

Result version number	v1 (current)
This version publication date	08 September 2022
First version publication date	08 September 2022

Trial information

Trial identification

Sponsor protocol code	RC19_0055

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03960801
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU NANTES
Sponsor organisation address	5 allée de l'ile gloriette, NANTES, France,
Public contact	Direction de la Recherche, CHU NANTES, 33 25348283533, bp-prom-reg@chu-nantes.fr
Scientific contact	Direction de la Recherche, CHU NANTES, 33 25348283533, bp-prom-reg@chu-nantes.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	08 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to demonstrate the non-inferiority of a rapid sequence anesthetic induction without curare with remifentanil on the prevention of major complications related to tracheal intubation compared to a rapid sequence induction with curare of short duration of action.

Protection of trial subjects:

The investigators are responsible for obtaining the written free and informed consent of the patient, after having provided him/her with information about the protocol .In case of impossibility for the investigators to deliver clear and loyal information to the patient within the maximum time of inclusion of the study (e.g.: urgent surgical procedure, polytrauma, confusional state), an emergency procedure was available to the investigator in order to support the inclusion of the patient without delaying the medical-surgical management

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2019
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: 1150
Worldwide total number of subjects	1150
EEA total number of subjects	1150

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)	840
From 65 to 84 years	308

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study population was composed of adult hospitalized patients requiring rapid sequence induction in the operating room or in the dechoking room.

Participation in the study was proposed to the patient during the preoperative anaesthesia consultation by the anaesthesiologist-intensive care physician, with the presentation of the information not

Pre-assignment

Screening details:

Subjects were included in few french hospital

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	REMIFENTANIL

Arm description:

Injection of remifentanil (3 to 4µg/kg) immediately after the injection of a hypnotic

Arm type	Experimental
Investigational medicinal product name	REMIFENTANIL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Injection of remifentanil (3 to 4µg/kg) immediately after the injection of a hypnotic

Arm title	MYORELAXANT

Arm description:

injection of rocuronium bromide or suxamethonium chloride

Arm type	Active comparator
Investigational medicinal product name	SUXAMETHONIUM CHLORIDE
Investigational medicinal product code	
Other name	succinylcholine
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

a rapid onset paralytic agent (1 mg/kg of succinylcholine was intravenously injected immediately after administering a hypnotic, and the tracheal intubation was initiated 30 to 60 seconds after administration of the myorelaxant. Succinylcholine was the myorelaxant first choice and rocuronium was recommended in case of counterindication of the use of succinylcholine. No morphine derivates should be injected before the first intubation attempt.

Investigational medicinal product name	ROCURONIUM CHLORIDE
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

a rapid onset paralytic agent (1 mg/kg of rocuronium) was intravenously injected immediately after administering a hypnotic, and the tracheal intubation was initiated 30 to 60 seconds after administration of the myorelaxant. Succinylcholine was the myorelaxant first choice and rocuronium was recommended in case of counterindication of the use of succinylcholine. No morphine derivates should be injected before the first intubation attempt.

Number of subjects in period 1	REMIFENTANIL	MYORELAXANT
Started	575	575
Completed	575	575

Baseline characteristics

Reporting groups

Reporting group title	Period 1

Reporting group description: -

Reporting group values	Period 1	Total	
Number of subjects	1150	1150	
Age categorical Units: Subjects			
Adults	1150	1150	
Gender categorical Units: Subjects			
Female	573	573	
Male	577	577	

Subject analysis sets

Subject analysis set title	Analysis ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

From October 2019 to April 2021, 1150 patients underwent randomization (egal ITT population) and were followed up for seven days (575 patients in the remifentanil group and 575 in the myorelaxant group).

Reporting group values	Analysis ITT		
Number of subjects	1150		
Age categorical Units: Subjects			
Adults	1150		
Gender categorical Units: Subjects			
Female	573		
Male	577		

End points

End points reporting groups

Reporting group title	REMIFENTANIL
Reporting group description:	
Injection of remifentanil (3 to 4µg/kg) immediately after the injection of a hypnotic	

Reporting group title	MYORELAXANT
Reporting group description:	
injection of rocuronium bromide or suxamethonium chloride	
Subject analysis set title	Analysis ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
From October 2019 to April 2021, 1150 patients underwent randomization (egal ITT population) and were followed up for seven days (575 patients in the remifentanil group and 575 in the myorelaxant group).	

Primary: successful tracheal intubation without major complications

End point title	successful tracheal intubation without major complications
End point description:	

End point type	Primary
End point timeframe:	
within 10 min after intubation	

End point values	REMIFENTANIL	MYORELAXANT	Analysis ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	566	570	1136	
Units: subjects	374	408	782	

Statistical analyses

Statistical analysis title	ITT analysis
Comparison groups	MYORELAXANT v REMIFENTANIL
Number of subjects included in analysis	1136
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Proportion difference
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-0.6

Adverse events

Adverse events information	
Timeframe for reporting adverse events: until end of hospitalization	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	All patients randomized

Reporting group description: -

Serious adverse events	All patients randomized		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 1150 (1.30%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Premature recovery from anaesthesia			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	4 / 1150 (0.35%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal necrosis			

subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vomiting				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Oxygen saturation decreased				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Trismus				
subjects affected / exposed	1 / 1150 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients randomized		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 1150 (3.04%)		
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences (all)	1		
Vascular disorders			
Haemodynamic instability			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	17 / 1150 (1.48%)		
occurrences (all)	17		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences (all)	1		
Extrasystoles			
subjects affected / exposed	1 / 1150 (0.09%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	4 / 1150 (0.35%)		
occurrences (all)	4		
General disorders and administration site conditions			

Immediate post-injection reaction subjects affected / exposed occurrences (all)	2 / 1150 (0.17%) 2		
Respiratory, thoracic and mediastinal disorders Bronchospasm subjects affected / exposed occurrences (all)	1 / 1150 (0.09%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 1150 (0.17%) 2		
Infections and infestations Peritonitis subjects affected / exposed occurrences (all) Infection subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all)	2 / 1150 (0.17%) 2 1 / 1150 (0.09%) 1 1 / 1150 (0.09%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2020	Modification of investigator list Modification of inclusion criteria
10 September 2020	change in manufacturer of remifentanil
03 December 2020	Change in investigator list Change in statistical analysis part

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported