Clinical trial results:
Sedation with sevoflurane versus propofol in patients with Acute Respiratory Distress Syndrome caused by COVID-19 infection

Summary

EudraCT number	2020-001379-34
Trial protocol	ES
Global end of trial date	31 March 2021

Results information

Result version number	v1 (current)
This version publication date	01 November 2022
First version publication date	01 November 2022

Trial information

Trial identification

Sponsor protocol code	SEVO-COVID19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04359862
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Instituto de Investigación Sanitaria INCLIVA
Sponsor organisation address	Avd. Menéndez Pelayo 4, acc, Valencia, Spain, 46010
Public contact	Subdirectora Científica, Instituto de Investigación Sanitaria INCLIVA, 0034 961973536, gestioncientifica@incliva.es
Scientific contact	Subdirectora Científica, Instituto de Investigación Sanitaria INCLIVA, 0034 961973536, gestioncientifica@incliva.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	18 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2021
Global end of trial reached?	Yes
Global end of trial date	31 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of 48-hour treatment with inhaled sevoflurane on arterial oxygenation, assessed by PaO2/FiO2 on day two, in patients with ARDS-CoVid19

Protection of trial subjects:

The protocol, informed consent form, participant information sheet and any applicable documents were submitted and approved by an appropriate Ethics Committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2020
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: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	8
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with Respiratory Distress caused by COVID19 Infection, admitted in the Anaesthesiology department and Intensive Care Unit of the participating hospitals.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	17
Number of subjects completed	

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SEVOFLURANE Group

Arm description:

25 patients sedated with Sevoflurane via inhalation, starting with 6 ml/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)

Arm type	Experimental
Investigational medicinal product name	SEVOFLURANE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, liquefied
Routes of administration	Inhalation use

Dosage and administration details:

starting dose 6 ml/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)

Arm title	PROPOFOL Group

Arm description:

25 patients standard sedation with intravenous propofol, starting with 2 mg/kg/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)

Arm type	Active comparator
Investigational medicinal product name	PROPOFOL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

starting dose 2 mg/kg/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)

Number of subjects in period 1	SEVOFLURANE Group	PROPOFOL Group
Started	7	10
Completed	7	10

Baseline characteristics

Reporting groups	
Reporting group title	SEVOFLURANE Group
Reporting group description:	
25 patients sedated with Sevoflurane via inhalation, starting with 6 ml/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)	
Reporting group title	PROPOFOL Group
Reporting group description:	
25 patients standard sedation with intravenous propofol, starting with 2 mg/kg/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)	

Reporting group values	SEVOFLURANE Group	PROPOFOL Group	Total
Number of subjects	7	10	17
Age categorical 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)	3	5	8
From 65-84 years	4	5	9
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	4	8
Male	3	6	9

End points

End points reporting groups

Reporting group title	SEVOFLURANE Group
Reporting group description:	
25 patients sedated with Sevoflurane via inhalation, starting with 6 ml/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)	
Reporting group title	PROPOFOL Group
Reporting group description:	
25 patients standard sedation with intravenous propofol, starting with 2 mg/kg/h and changing every 15 minutes until an adequate level of sedation is achieved (BIS 40-50)	

Primary: To evaluate the effect on arterial oxygenation of treatment with inhaled sevoflurane for 48 hours, evaluated by PaO2/FiO2 on the second day, in patients with Acute Respiratory Distress Syndrome caused by COVID-19 infection.

End point title	To evaluate the effect on arterial oxygenation of treatment with inhaled sevoflurane for 48 hours, evaluated by PaO2/FiO2 on the second day, in patients with Acute Respiratory Distress Syndrome caused by COVID-19 infection.
End point description:	
Difference in PaO2/FiO2 at 48-hour between Sevofluorane and Propofol arms.	
End point type	Primary
End point timeframe:	
Selection, Visit 1 (24h) and Visit 2 (48h)	

End point values	SEVOFLURANE Group	PROPOFOL Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: mmHg/%				
number (not applicable)	7	10		

Statistical analyses

Statistical analysis title	linear mixed regression model
Statistical analysis description:	
Continuous variables are expressed as means (±1 SD) or medians (interquartile range [IQR]), and discrete variables as percentages. At baseline, the comparisons of means, medians, and frequencies among treatment groups were carried out using the t-test, Wilcoxon test, and chi-square test, respectively. A linear mixed regression model (LMRM) was used for the analysis of the primary endpoint. We modeled changes from baseline in PaO2/FiO2 as a longitudinal outcome. Because of hierarchical levels of	
Comparison groups	SEVOFLURANE Group v PROPOFOL Group

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA

Secondary: Assess mortality at 30 days

End point title	Assess mortality at 30 days

End point description:

All-cause mortality evaluated at 30 days

End point type	Secondary

End point timeframe:

Administrative censoring was applied at 30-day after randomization. Total follw-up was 30 days.

End point values	SEVOFLURANE Group	PROPOFOL Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: days	7	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
During the patient's participation in the study	
Adverse event reporting additional description:	
No adverse events occurred during the course of the study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	4

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

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 adverse events occurred during the course of the study

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2020	Protocol modification version 2.0 15 april 2020

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported