Clinical trial results:
A phase IV randomized, controlled clinical trial to compare the high flow oxygen therapy (group of intervention) opposite to the conventional oxygen therapy (group control) in patients with severe acute respiratory failure.

Summary

EudraCT number	2012-001671-36
Trial protocol	ES
Global end of trial date	01 October 2015

Results information

Result version number	v1 (current)
This version publication date	16 February 2022
First version publication date	16 February 2022
Summary attachment (see zip file)	Paper Optiflow (Therapeutic Advances in respiratory disease.pdf)

Trial information

Trial identification

Sponsor protocol code	EC11-103

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fundación de Investigación Biomédica (FIB) del Hospital Universitario de La Princesa
Sponsor organisation address	Calle Diego de León, 62, Madrid, Spain, 28006
Public contact	Dpto.EECC, Fundación para la Investigación Biomédica, 34 915202476, eecc.fib.hlpr@salud.madrid.org
Scientific contact	Dpto.EECC, Fundación para la Investigación Biomédica, 34 915202476, eecc.fib.hlpr@salud.madrid.org

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	31 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2015
Global end of trial reached?	Yes
Global end of trial date	01 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To Evaluate if the high flow oxigen therapy with warm system of humidificación by means of nasal glasses (optiflow) opposite to the conventional oxygen therapy like treatment of the severe acute respiratory failure of any etiology determines a minor need of intubation orotraqueal
2. To evaluate if the system optiflow provides a better tolerance and comfort of the patient with severe acute respiratory failure that needs oxygen therapy to high concentrations of oxygen.

Protection of trial subjects:

The information disseminated and obtained through the implementation of this study is considered confidential and should be treated as such at all times. Study subjects will be identified by the initial letter of their name followed by the subject number in the study. Both the investigators responsible of the clinical trial, as well as a representative of the sponsor or of the Health Authorities, will have access to the information the information recorded throughout the study. In case of publication of the results of the study, the identity of the patients will not be revealed.

Background therapy: -

Evidence for comparator:

Conventional oxygen therapy: venturi mask with FiO2 between 60 and 100%

Actual start date of recruitment	15 January 2013
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: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	46
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in the Intensive Care Unit (ICU), University Hospital La Princesa in Madrid (Spain) between January 2013 and December 2015.

Pre-assignment

Screening details:

Patients older than 18 years, of both sexes, with AHRF of any etiology after signing informed consent. AHRF was defined as: a PaO2/FIO2 ratio 200 or SpO2/FIO2 ratio 160 (SpO2 = peripheral oxygen saturation by pulse oximetry); and respiratory rate > 30 r/min for at least 30 min.

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	High-flow nasal cannula (HFNC)

Arm description:

It provides high flow, matching the patient’s inspiratory flow demands, at an ideal temperature and humidity, which improves oxygenation, produces a certain continuous positive pressure effect on airways, reduces proximal airway dead space, and increases respiratory volumes.

Arm type	Experimental
Investigational medicinal product name	Optiflow
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	External use

Dosage and administration details:

Oxygen 50l/min

Arm title	Conventional oxygen therapy (COT)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ventimask
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	External use

Dosage and administration details:

Oxygen FiO2 60-100%

Number of subjects in period 1	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)
Started	24	22
24 hours	24	22
Completed	24	22

Baseline characteristics

Reporting groups	
Reporting group title	High-flow nasal cannula (HFNC)

Reporting group description:

It provides high flow, matching the patient’s inspiratory flow demands, at an ideal temperature and humidity, which improves oxygenation, produces a certain continuous positive pressure effect on airways, reduces proximal airway dead space, and increases respiratory volumes.

Reporting group title	Conventional oxygen therapy (COT)

Reporting group description: -

Reporting group values	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)	Total
Number of subjects	24	22	46
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58	61	
standard deviation	± 19	± 11	-
Gender categorical Units: Subjects			
Female	11	9	20
Male	13	13	26

End points

End points reporting groups

Reporting group title	High-flow nasal cannula (HFNC)
Reporting group description:	
It provides high flow, matching the patient’s inspiratory flow demands, at an ideal temperature and humidity, which improves oxygenation, produces a certain continuous positive pressure effect on airways, reduces proximal airway dead space, and increases respiratory volumes.	
Reporting group title	Conventional oxygen therapy (COT)
Reporting group description: -	

Primary: Intubation

End point title	Intubation
End point description:	
End point type	Primary
End point timeframe:	
Overall	

End point values	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: 22	8	14		

Statistical analyses

Statistical analysis title	Statistical analysis Intubation
Statistical analysis description:	
A descriptive analysis was carried out, analyzing the comparability of the groups and comparing by intention to treat: bivariate (parametric or nonparametric) and multivariate (linear regression for repeated measures or Cox proportional risk regression).	
Comparison groups	High-flow nasal cannula (HFNC) v Conventional oxygen therapy (COT)
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard

Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Primary: Discomfort

End point title	Discomfort

End point description:

Of the 24 HFNC group patients, 3 subjects did not tolerate the device because of the displeasing heat.

End point type	Primary

End point timeframe:

Overall

End point values	High-flow nasal cannula (HFNC)	Conventional oxygen therapy (COT)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: 24	3	0		

Statistical analyses

Statistical analysis title	Statistical analysis Discomfort

Statistical analysis description:

A descriptive analysis was carried out, analyzing the comparability of the groups and comparing by intention to treat: bivariate (parametric or nonparametric)
and multivariate (linear regression for repeated measures or Cox proportional risk regression).

Comparison groups	High-flow nasal cannula (HFNC) v Conventional oxygen therapy (COT)
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Prospective follow-up will be carried out until hospital discharge or exitus, or if orotracheal intubation is necessary without orotracheal intubation unrelated to respiratory failure (coma of other etiology, surgery, cerebral arteriography, etc.)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	HFNC

Reporting group description: -

Serious adverse events	HFNC		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	HFNC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 24 (87.50%)		
Injury, poisoning and procedural complications			
Exposure to noise			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	24		
Exposure to heat			
subjects affected / exposed	17 / 24 (70.83%)		
occurrences (all)	24		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The principal limitation was that participation was offered to one-third of eligible patiens

Notes: