Clinical trial results:
(Feasibility) Open label Randomised Controlled Trial of Hyperoxic O2 Therapy vs. Normoxic O2 Therapy in Sepsis

Summary

EudraCT number	2015-000629-35
Trial protocol	GB
Global end of trial date	10 November 2016

Results information

Result version number	v1 (current)
This version publication date	31 May 2019
First version publication date	31 May 2019

Trial information

Trial identification

Sponsor protocol code	Version 2.2; March 2016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02378545
WHO universal trial number (UTN)	-
Other trial identifiers	IRAS No.: 171788, R&D No.: 15/P/020, REC No.: 15/WM/0175

Notes:

Sponsors

Sponsor organisation name	University Hospitals Plymouth NHS Trust (previously known as Plymouth Hospitals NHS Trust)
Sponsor organisation address	Research Office, L2 MSCP, Bircham Park Offices, 1 Roscoff Rise, Derriford, Plymouth, United Kingdom, PL6 5FP
Public contact	Dr Chris Rollinson, Research Governance Mananger, University Hospitals Plymouth NHS Trust, 01752 432842, c.rollinson@nhs.net
Scientific contact	Dr Tim Nutbeam, Consultant in Emergency Medicine, University Hospitals Plymouth NHS Trust, 01752 437629, timnutbeam@nhs.net

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	10 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2016
Global end of trial reached?	Yes
Global end of trial date	10 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the feasibility of a study which answers the question: "In adult patients with sepsis presenting to the emergency department by ambulance does delivery of high flow oxygen (hyperoxic oxygen therapy) compared to titrated (normoxic) oxygen therapy reduce mortality at 90 days"

NB. Mortality at 90 days (note: this is a feasibility study, multiple outcomes are of relevance in informing the definitive study).

Protection of trial subjects:

The study is approved by the MHRA and the West Midlands - Edgbaston Research Ethics Committee (NRES). Study monitoring is conducted by UHPNT and an Independent Trial Steering Committee (TSC), Trial Management Group (TMG) and Data Monitoring Committee (DMC) are set up for the study oversight.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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	United Kingdom: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	19
From 65 to 84 years	25
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Patients with sepsis arriving by ambulance to Derriford Emergency Department. Routine assessment confirms patient has possible sepsis (SIRS + presence of infection). Patient assessed for the trial eligibility. If eligible informed consent is taken. Patient randomised to receive either Hyperoxia or Normoxia.

Pre-assignment

Screening details:

Patients with baseline observations outside of the normal limits will be screened for trial participation. Screening consists of a 4 steps: Is SIRS present? Does the participant have an active or presumed Infection? Is a sepsis MIMIC more likely to be the cause of this participant's presentation to hospital? Do any other EXCLUSION criteria exist?

Pre-assignment period milestones

Number of subjects started	50
Number of subjects completed	50

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Hyperoxia

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Oxygen (Hyperoxia)
Investigational medicinal product code	
Other name	Medical Oxygen
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

Oxygen will be administered using a non-re-breathe oxygen mask applied over the face and nose. The oxygen delivery device will be set to deliver oxygen at 15 litres per minute. The oxygen will be continuously delivered throughout the patients stay in the Emergency Department.

Arm title	Normoxia

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Oxygen (normoxia)
Investigational medicinal product code	
Other name	Medical Oxygen
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

Oxygen will not be administered if a patient's oxygen saturations (as measured using a pulse oximeter) are 94%. If a patient's oxygen saturations are less than 94%, oxygen will be 'titrated' using a 'venturi' type oxygen delivery device to achieve target saturations of 94%. Following initial dynamic titration (to identify correct oxygen delivery level) the oxygen delivery device will be re-evaluated hourly during the

patient’s stay in the emergency department.

Number of subjects in period 1	Hyperoxia	Normoxia
Started	25	25
Completed	25	25

Baseline characteristics

Reporting groups	
Reporting group title	Hyperoxia
Reporting group description: -	
Reporting group title	Normoxia
Reporting group description: -	

Reporting group values	Hyperoxia	Normoxia	Total
Number of subjects	25	25	50
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	69.32	59.12	
standard deviation	± 16.64	± 22.83	-
Gender categorical Units: Subjects			
Female	18	12	30
Male	7	13	20

End points

End points reporting groups

Reporting group title	Hyperoxia
Reporting group description: -	
Reporting group title	Normoxia
Reporting group description: -	

Primary: Mortality at 90 days

End point title	Mortality at 90 days[1]

End point description:

The primary endpoint/outcome is mortality at 90 days. This is a feasibility study, multiple outcomes are of relevance in informing the definitive study: Can the study procedures be implemented as planned; Recruitment rate, characteristics of patients not recruited; Drop-out rate and reasons for drop out; Data collection success / missing data; Additional currently unidentified costs; Adequacy of follow up arrangements / number of patients lost to follow up; Collect data to identify survival and quality of life differences which may inform power calculation and primary outcome for the definitive study; Optimal hours for patient recruitment; Identification of unexpected adverse events / reactions; Identify patients for patient and public involvement.

End point type	Primary

End point timeframe:

Visit 4 - follow up at 90 days.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study is a feasibility study using descriptive statistics, therefore not powered to complete inferential statistics.

End point values	Hyperoxia	Normoxia		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	23		
Units: Number of people	25	23		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All SAEs, SARs including SUSARs are reported to the RD Office (sponsor) within 24 hours. RD Office to report to MHRA and REC within 7 days if fatal or life-threatening and all other SUSARs within 15 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

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: This patient group had sepsis and were seriously ill and incapacitated. No adverse events were reported at the 90 day follow-up.

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