



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 Manager, 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

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|--------------------|----|
| 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