



## Clinical trial results:

### Can muscle dysfunction in COPD be altered by oxygenation in patients with intermittent hypoxia on exertion?

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2011-003595-36   |
| Trial protocol           | GB               |
| Global end of trial date | 15 December 2014 |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)                                     |
| This version publication date     | 04 January 2020                                  |
| First version publication date    | 04 January 2020                                  |
| Summary attachment (see zip file) | Summary Results (Abstract of trial results.docx) |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | ERN_11-0670 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01722370 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University of Birmingham  |
| Sponsor organisation address | Edgbaston, Birmingham, United Kingdom,                                    |
| Public contact               | Alice Wood, University of Birmingham, +44 1214143344, a.m.wood@bham.ac.uk |
| Scientific contact           | Alice Wood, University of Birmingham, +44 1214143344, a.m.wood@bham.ac.uk |

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                       | 01 December 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 15 December 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 15 December 2014 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Our primary question is whether changes in muscle structure including gene expression occur during normal daily life in patients with COPD that can be corrected by giving oxygen. To do this we will compare the appearance of and genes expressed in muscle of patients after they have received oxygen and after they have been given air to use at home for 12 weeks.

Protection of trial subjects:

Local anaesthetic was used for biopsies

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 23 January 2012 |
| 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 | United Kingdom: 25 |
| Worldwide total number of subjects   | 25                 |
| EEA total number of subjects         | 25                 |

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)                      | 2  |
| From 65 to 84 years                       | 23 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

recruited between September 2012 and August 2014 in single site in England

### Pre-assignment

Screening details:

32 subjects screened for inclusion of whom 25 recruited. All participants had completed pulmonary rehabilitation within 2 years prior to trial enrolment and demonstrated exercise induced desaturation to a nadir <88%.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | ambulatory oxygen       |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

Blinding implementation details:

Sealed envelope

### Arms

|                              |    |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | ambulatory oxygen |
|------------------|-------------------|

Arm description:

oxygen used on walking

|  |                   |
|--|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | oxygen            |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Inhalation vapour |
| Routes of administration               | Inhalation use    |

Dosage and administration details:

Oxygen 2l/min or as required to maintain saturations

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | ambulatory air |
|------------------|----------------|

Arm description:

Air breathed from a cylinder blinded to look same as oxygen when walking

|  |                   |
|--|-------------------|
| Arm type                               | Placebo           |
| Investigational medicinal product name | medical air       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Inhalation vapour |
| Routes of administration               | Inhalation use    |

Dosage and administration details:

Medical air given by cylinder used when walking

| <b>Number of subjects in period 1</b> | ambulatory oxygen | ambulatory air |
|---------------------------------------|-------------------|----------------|
| Started                               | 13                | 12             |
| Completed                             | 10                | 7              |
| Not completed                         | 3                 | 5              |
| Physician decision                    | 1                 | -              |
| Consent withdrawn by subject          | -                 | 4              |
| Lost to follow-up                     | 2                 | 1              |

## Period 2

|                                  |                         |
|----------------------------------|-------------------------|
| Period 2 title                   | medical air             |
| Is this the baseline period?     | No                      |
| Allocation method                | Randomised - controlled |
| Blinding used                    | Double blind            |
| Roles blinded                    | Subject, Investigator   |
| Blinding implementation details: |                         |
| Sealed envelope                  |                         |

## Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | No                |
| <b>Arm title</b>             | ambulatory oxygen |

Arm description:

oxygen used on walking

|  |                   |
|--|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | oxygen            |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Inhalation vapour |
| Routes of administration               | Inhalation use    |

Dosage and administration details:

Oxygen 2l/min or as required to maintain saturations

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | ambulatory air |
|------------------|----------------|

Arm description:

Air breathed from a cylinder blinded to look same as oxygen when walking

|  |                   |
|--|-------------------|
| Arm type                               | Placebo           |
| Investigational medicinal product name | medical air       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Inhalation vapour |
| Routes of administration               | Inhalation use    |

Dosage and administration details:

Medical air given by cylinder used when walking

| <b>Number of subjects in period 2</b> | ambulatory oxygen | ambulatory air |
|---------------------------------------|-------------------|----------------|
| Started                               | 13                | 12             |
| Completed                             | 10                | 7              |
| Not completed                         | 3                 | 5              |
| Physician decision                    | 1                 | -              |
| Consent withdrawn by subject          | -                 | 4              |
| Lost to follow-up                     | 2                 | 1              |

## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | ambulatory oxygen |
|-----------------------|-------------------|

Reporting group description:

oxygen used on walking

|                       |                |
|-----------------------|----------------|
| Reporting group title | ambulatory air |
|-----------------------|----------------|

Reporting group description:

Air breathed from a cylinder blinded to look same as oxygen when walking

| Reporting group values                                | ambulatory oxygen | ambulatory air | Total |
|---|-------------------|----------------|-------|
| Number of subjects                                    | 13                | 12             | 25    |
| Age categorical                                       |                   |                |       |
| Units: Subjects                                       |                   |                |       |
| In utero  | 0                 | 0              | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                 | 0              | 0     |
| Newborns (0-27 days)                                  | 0                 | 0              | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0                 | 0              | 0     |
| Children (2-11 years)                                 | 0                 | 0              | 0     |
| Adolescents (12-17 years)                             | 0                 | 0              | 0     |
| Adults (18-64 years)                                  | 1                 | 1              | 2     |
| From 65-84 years                                      | 12                | 11             | 23    |
| 85 years and over                                     | 0                 | 0              | 0     |
| Age continuous  |                   |                |       |
| Units: years  |                   |                |       |
| arithmetic mean                                       | 67.35             | 66.45          |       |
| standard deviation                                    | ± 7.45            | ± 6.52         | -     |
| Gender categorical                                    |                   |                |       |
| Units: Subjects                                       |                   |                |       |
| Female  | 7                 | 6              | 13    |
| Male  | 6                 | 6              | 12    |

## End points

### End points reporting groups

|                              |  |
|------------------------------|--|
| Reporting group title        | ambulatory oxygen  |
| Reporting group description: | oxygen used on walking   |
| Reporting group title        | ambulatory air   |
| Reporting group description: | Air breathed from a cylinder blinded to look same as oxygen when walking |
| Reporting group title        | ambulatory oxygen  |
| Reporting group description: | oxygen used on walking   |
| Reporting group title        | ambulatory air   |
| Reporting group description: | Air breathed from a cylinder blinded to look same as oxygen when walking |

### Primary: Gene expression

|                        |   |
|------------------------|---|
| End point title        | Gene expression   |
| End point description: | Not possible to give a single value as gene expression obtained for whole genome and analysed as gene set enrichment analyses, hence data inserted in this record entered as 1.0 to allow record completion. Data set can be found at <a href="https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE90154">https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE90154</a> |
| End point type         | Primary   |
| End point timeframe:   | Compared between 12 weeks ambulatory oxygen and 12 weeks air.   |

| End point values                     | ambulatory oxygen | ambulatory air  | ambulatory oxygen | ambulatory air  |
|--------------------------------------|-------------------|-----------------|-------------------|-----------------|
| Subject group type                   | Reporting group   | Reporting group | Reporting group   | Reporting group |
| Number of subjects analysed          | 10                | 7               | 10                | 7               |
| Units: IU                            |                   |                 |                   |                 |
| arithmetic mean (standard deviation) | 1.0 (± 1.0)       | 1.0 (± 1.0)     | 1.0 (± 1.0)       | 1.0 (± 1.0)     |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Comparison of gene expression oxygen v air |
| Comparison groups                       | ambulatory oxygen v ambulatory air         |
| Number of subjects included in analysis | 17   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           | superiority <sup>[1]</sup>                 |
| P-value                                 | = 0.9 <sup>[2]</sup>                       |
| Method                                  | Significance Analysis of Microarrays (SA   |

Notes:

[1] - No significant differences in any individual gene .At a single gene level differential expression between ambulatory oxygen and air was not detectable.

[2] - Many p values are obtained as this is genomewide, this is the average

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### Secondary: Change in 6MWT distance

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|                 |                         |
|-----------------|-------------------------|
| End point title | Change in 6MWT distance |
|-----------------|-------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Compared between 12 weeks intervention and 12 weeks air, reported as change between periods (only one arm as crossed over)

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| End point values                     | ambulatory oxygen | ambulatory air  | ambulatory oxygen | ambulatory air  |
|--------------------------------------|-------------------|-----------------|-------------------|-----------------|
| Subject group type                   | Reporting group   | Reporting group | Reporting group   | Reporting group |
| Number of subjects analysed          | 10                | 7               | 10                | 7               |
| Units: meters                        |                   |                 |                   |                 |
| arithmetic mean (standard deviation) | 34.06 (± 125.33)  | 16.25 (± 99.25) | 34.06 (± 125.33)  | 16.25 (± 99.25) |

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### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 weeks oxygen treatment, 12 weeks air

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | ambulatory oxygen |
|-----------------------|-------------------|

Reporting group description:

oxygen used on walking

|                       |                |
|-----------------------|----------------|
| Reporting group title | ambulatory air |
|-----------------------|----------------|

Reporting group description:

Air breathed from a cylinder blinded to look same as oxygen when walking

| <b>Serious adverse events</b>                     | ambulatory oxygen | ambulatory air |  |
|---|-------------------|----------------|--|
| Total subjects affected by serious adverse events |                   |                |  |
| subjects affected / exposed                       | 0 / 25 (0.00%)    | 0 / 25 (0.00%) |  |
| number of deaths (all causes)                     | 0                 | 0              |  |
| number of deaths resulting from adverse events    | 0                 | 0              |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | ambulatory oxygen                                       | ambulatory air |  |
|---|---|----------------|--|
| Total subjects affected by non-serious adverse events |   |                |  |
| subjects affected / exposed                           | 0 / 25 (0.00%)  | 1 / 25 (4.00%) |  |
| Respiratory, thoracic and mediastinal disorders       |   |                |  |
| Epistaxis   | Additional description: Small nose bleed, self limiting |                |  |
| subjects affected / exposed                           | 0 / 25 (0.00%)  | 1 / 25 (4.00%) |  |
| occurrences (all)                                     | 0   | 1              |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported