



Clinical trial results:

Randomised, controlled crossover trial to evaluate the Effects of Ambulatory Oxygen on health status in patients with Fibrotic Lung Disease (FLD)

Summary

EudraCT number	2013-004355-20
Trial protocol	GB
Global end of trial date	15 September 2017

Results information

Result version number	v1 (current)
This version publication date	17 October 2019
First version publication date	17 October 2019
Summary attachment (see zip file)	AmbOxy Publication (Ambulatory Oxygen publication.pdf)

Trial information

Trial identification

Sponsor protocol code	2013OE005B
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Royal Brompton and Harefield NHS Foundation Trust
Sponsor organisation address	Sydney Street, LONDON, United Kingdom,
Public contact	Ira Jakupovic, Royal Brompton and Harefield NHS Foundation Trust , 44 2073518109, i.jakupovic@rbht.nhs.uk
Scientific contact	Ira Jakupovic, Royal Brompton and Harefield NHS Foundation Trust , 44 2073518109, i.jakupovic@rbht.nhs.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	20 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2017
Global end of trial reached?	Yes
Global end of trial date	15 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main symptom that occurs in fibrotic lung disease (lung scarring) is breathlessness due to the progressive scarring of the lungs, with a profound impact on daily activities. During exercise, lung fibrosis is often associated with a drop in oxygen saturation which can be corrected by the use of supplemental oxygen. In patients with lung scarring, the main cause of overall worsening quality of life is breathlessness.

The principal research question is the study of the impact of supplemental oxygen on health status. We strongly believe that attempts to improve or maintain health status are of crucial importance, especially in this group of respiratory diseases, characterized overall by a poor prognosis and progressive worsening in quality of life.

Protection of trial subjects:

SAEs were monitored by IDMC

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2014
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: 84
Worldwide total number of subjects	84
EEA total number of subjects	84

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)	28
From 65 to 84 years	55
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

269 subjects were screened; 171 excluded; 125 ineligible and 46 declined; 98 completed screening visit;

Period 1

Period 1 title	Randomisation (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	No
Arm title	Oxygen

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Cylinders weight range 1.8-2.2 kg

Arm title	Non-Oxygen
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Arm description: -

Arm type	comparator
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Oxygen	Non-Oxygen
Started	41	43
Completed	37	39
Not completed	4	4
Adverse event, serious fatal	1	1
Consent withdrawn by subject	2	1
Adverse event, non-fatal	-	2
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Randomisation
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Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	84	84	
Age categorical			
Units: Subjects			
Adults (18-64 years)	28	28	
From 65-84 years	55	55	
85 years and over	1	1	
Gender categorical			
Units: Subjects			
Female	26	26	
Male	58	58	

End points

End points reporting groups

Reporting group title	Oxygen
Reporting group description: -	
Reporting group title	Non-Oxygen
Reporting group description: -	

Primary: K-BILD score

End point title	K-BILD score
End point description:	
End point type	Primary
End point timeframe:	
At the end of the cross over.	

End point values	Oxygen	Non-Oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	39		
Units: 00.00	37	39		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
For the primary outcome, a generalised linear model was used with the difference in HRQOL as the dependent variable and treatment sequence as a fixed effect. An adjustment was made for the order of treatment. The same method was used to analyse the secondary outcomes. Conditional logistic regression, with sequence as an interaction term, was used to analyse the effects of oxygen on the presence of anxiety or depression. All the analysis was by intention to treat. Significance was at $p < 0.05$	
Comparison groups	Oxygen v Non-Oxygen
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	generalised linear model
Parameter estimate	Mean difference (final values)
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.6

<div>Variability estimate</div>	<div>Standard deviation</div>
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Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:
within 24 hours of their becoming aware of the event

Assessment type	Systematic
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Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Oxygen
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Reporting group description: -

Reporting group title	No Oxygen
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Reporting group description: -

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 study was based on utilizing routine standard of care in this patient group, and the design was based on cross over, ensuring that patients in both arms received ambulatory oxygen and the time of being in the relevant study arm. While the Sponsor had requested recording of non-serious adverse events in patient notes, we have only collected SAEs for this study.

Serious adverse events	Oxygen	No Oxygen	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	3 / 43 (6.98%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Angina			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chest infection			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia			

subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Dyspnoea			
subjects affected / exposed	1 / 41 (2.44%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Oxygen	No Oxygen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 43 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2015	- Changes to the study protocol to address the issues highlighted during monitoring visits - PIS and ICF changed to ensure consistency with the study protocol REC FAO 13.01.2015 MHRA Approval 19.01.2015
09 November 2015	- The Substantial Amendment proposes to add a new site to the study: North Bristol NHS Trust, PI Dr Huzaifa Adamali REC FAO 09.11.2015

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported