Clinical trial results:
TARGETING OF THE SMALL AIRWAYS IN PATIENTS WITH COPD: AIRWAY EFFECTS OF TIOTROPIUM -Respimat vs. Handihaler

Summary

EudraCT number	2015-001615-13
Trial protocol	GB
Global end of trial date	11 January 2018

Results information

Result version number	v1 (current)
This version publication date	19 October 2019
First version publication date	19 October 2019

Trial information

Trial identification

Sponsor protocol code	151C2697

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02683668
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
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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	07 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2018
Global end of trial reached?	Yes
Global end of trial date	11 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Our principle objective is to investigate the effect of tiotropium (a long-acting inhaled bronchodilator), delivered from different devices, on a panel of small (IOS, MBNW, DLCO, FVC) and large airway (FEV1, PEF) responses in patients with mild-moderate COPD. We will compare equivalent doses of Titropium from Respimat (Tiotropium Respimat 5 micrograms once daily), a small particle soft mist inhaler (SMI) compared to delivering it from Handihaler (18 micrograms once daily), a standard large particle dry powder inhaler (DPI). Respimat is a novel inhaler platform that has small particles and a slow inhalation allowing deeper lung drug delivery.

We will be using easily performed non-invasive breathing tests to measure response:
- Impulse Oscillometry (IOS) parameters
- Multiple Nitrogen Washout parameters (MBNW)
- Lung function test (LFT) parameters:

We will also assess the safety and tolerability, as determined by vital signs of heart rate and blood pressure.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2015
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: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	12
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participant were recruited at Royal Brompton Hospital between February 2016 and January 2018

Pre-assignment

Screening details:

A total of 47 participant were screened, 3 excluded due to not meet the inclusion criteria

Period 1

Period 1 title	Phase 0
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All participant

Arm description:

All participants treated with HandiHaler 18mcg Tiotropium, no training for the participants

Arm type	Experimental
Investigational medicinal product name	Tiotropium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

18ug daily

Number of subjects in period 1	All participant
Started	44
Completed	44

Period 2

Period 2 title	Phase 1
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All participant

Arm description:

All participant treated with HandiHaler 18ug Tiotropium daily. training provided for participants

Arm type	Experimental
Investigational medicinal product name	Tiotropium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

18ug daily

Number of subjects in period 2	All participant
Started	44
Completed	43
Not completed	1
Consent withdrawn by subject	1

Period 3

Period 3 title	phase 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All participant

Arm description:

All participants treated with Respimat 5mcg Tiotropium, no training for the participants

Arm type	Experimental
Investigational medicinal product name	Tiotropium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

5ug daily

Number of subjects in period 3	All participant
Started	43
Completed	43

Baseline characteristics

Reporting groups	
Reporting group title	Phase 0

Reporting group description: -

Reporting group values	Phase 0	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
From 65-84 years	32	32	
Age continuous Units: years			
geometric mean	69.1		
standard deviation	± 8.0	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	23	23	
R5-R20 Peripheral Airways Resistance Units: kPal/s			
arithmetic mean	0.608		
standard deviation	± 0.207	-	

End points

End points reporting groups

Reporting group title	All participant
Reporting group description:	
All participants treated with HandiHaler 18mcg Tiotropium, no training for the participants	
Reporting group title	All participant
Reporting group description:	
All participant treated with HandiHaler 18ug Tiotropium daily. training provided for participants	
Reporting group title	All participant
Reporting group description:	
All participants treated with Respimat 5mcg Tiotropium, no training for the participants	

Primary: R5-R20

End point title	R5-R20[1]
End point description:	
End point type	Primary
End point timeframe:	
6 months	

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: Statistical analyses ongoing, end date is January 2020.

End point values	All participant	All participant	All participant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	43	43	
Units: kPal/s				
arithmetic mean (standard deviation)	0.608 (± 0.207)	0.589 (± 0.169)	0.497 (± 0.148)	

Statistical analyses

No statistical analyses for this end point

Primary: Sacin

End point title	Sacin[2]
End point description:	
After treatment IMPULSE Oscillometry	
End point type	Primary
End point timeframe:	
14 days	

Notes:

[2] - 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: Statistical analyses ongoing, end date is January 2020.

End point values	All participant	All participant	All participant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	43	43	
Units: kPal\s				
arithmetic mean (standard deviation)	0.333 (± 0.103)	0.339 (± 0.119)	0.345 (± 0.134)	

Statistical analyses

No statistical analyses for this end point

Primary: Lung function FEV1

End point title	Lung function FEV1[3]

End point description:

End point type	Primary

End point timeframe:

14 days

Notes:

[3] - 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: Statistical analyses ongoing, end date is January 2020.

End point values	All participant	All participant	All participant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	43	43	
Units: litre(s)				
arithmetic mean (standard deviation)	1.575 (± 0.483)	1.571 (± 0.523)	1.651 (± 0.497)	

Statistical analyses

No statistical analyses for this end point

Secondary: Multi-Breath Washout Test (MBW)

End point title	Multi-Breath Washout Test (MBW)

End point description:

End point type	Secondary

End point timeframe:

14 days

End point values	All participant	All participant	All participant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	43	43	
Units: kPal/s				
arithmetic mean (standard deviation)	0.047 (± 0.042)	0.042 (± 0.032)	0.036 (± 0.032)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

3 months

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	All participant

Reporting group description: -

Serious adverse events	All participant		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All participant		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)		

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: No adverse event were detected on the trial.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2015	Modify Participant consent form, Participant information sheet (PIS).
01 September 2016	We request a change in one of the exclusion criteria of our study protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported