Clinical trial results:
A Randomized, Double-Blind, Two Treatment, Two Period, Chronic Dosing (2 Weeks), Cross-Over, Multi-Center Study to Evaluate the Effects of PT001 and PT005 on Specific Image Based Airway Volumes and Resistance in Subjects With Moderate to Severe COPD.

Summary

EudraCT number	2015-001744-11
Trial protocol	BE
Global end of trial date	28 May 2018

Results information

Result version number	v1 (current)
This version publication date	15 June 2019
First version publication date	15 June 2019

Trial information

Trial identification

Sponsor protocol code	PT003019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02937548
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	N/A, N/A, Sweden,
Public contact	Stephan Stenglein, MD, AstraZeneca, +46 031 776 1000, stephan.stenglein@astrazeneca.com
Scientific contact	Stephan Stenglein, MD, AstraZeneca, +46 031 776 1000, stephan.stenglein@astrazeneca.com

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	28 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2018
Global end of trial reached?	Yes
Global end of trial date	28 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the Effects of PT001 and PT005 on Specific Image Based Airway Volumes and Resistance in Subjects With Moderate to Severe COPD.

Protection of trial subjects:

For subjects that were on ICS LABA, the ICS LABA was discontinued, however, then prescribed an ICS Monotherapy at an equivalent dosing regimen for the duration of the study. For subjects that were on ICS Monotherapy, they were allowed to continue those medications at the same dose. Ventolin HFA was provided throughout the study for subjects to take as needed for relief of symptoms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 December 2016
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	Belgium: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	8
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study randomized 23 subjects at 2 sites in Belgium from December 2016 to May 2018.

Pre-assignment

Screening details:

Subjects were randomized into 1 of 2 treatment sequences. Sequence 1 received GP MDI in Period 1 followed by FF MDI in Period 2. Sequence 2 received FF MDI in Period 1 followed by GP MDI in Period 2.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Subject, Assessor

Arms

Arm title	Overall Study

Arm description:

All Subjects Randomized

Arm type	Experimental
Investigational medicinal product name	Glycopyrronium Metered Dose Inhalation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation, suspension
Routes of administration	Inhalation use

Dosage and administration details:

Glycopyrronium Metered Dose Inhalation 14.4 µg

Investigational medicinal product name	Formoterol Fumarate Metered Dose Inhalation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation, suspension
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol Fumarate Metered Dose Inhalation 9.6 µg

Number of subjects in period 1	Overall Study
Started	23
Treated with GP MDI	20
Treated with FF MDI	22
Completed	19
Not completed	4
Adverse event, non-fatal	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description: -	

Reporting group values	Overall Study	Total	
Number of subjects	23	23	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	15	15	
85 years and over	0	0	
Age Continuous Units: years			
median	64.6		
standard deviation	± 9.6	-	
Sex: Female, Male Units: Subjects			
Female	6	6	
Male	17	17	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	23	23	
More than one race	0	0	
Unknown or Not Reported	0	0	

Subject analysis sets	
Subject analysis set title	GP MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Subjects Randomized	
Subject analysis set title	FF MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Subjects Randomized	

Reporting group values	GP MDI	FF MDI	
Number of subjects	20	22	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	8	
From 65-84 years	13	14	
85 years and over	0	0	
Age Continuous Units: years			
median	64.7	64.0	
standard deviation	± 9.4	± 9.4	
Sex: Female, Male Units: Subjects			
Female	4	5	
Male	16	17	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	20	22	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Overall Study
Reporting group description: All Subjects Randomized	
Subject analysis set title	GP MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Subjects Randomized	
Subject analysis set title	FF MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description: All Subjects Randomized	

Primary: Specific Image-Based Airway Volume (siVaw)

End point title	Specific Image-Based Airway Volume (siVaw)[1]
End point description: Specific image-based airway volume. Average across lobe, adjusted for lobe volume. Ratio to baseline	
End point type	Primary
End point timeframe: Day 15	

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: Data not available in compatible format to enter statistical analysis.

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	19	19	
Units: mL/L				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	1.11 (1.02 to 1.22)	1.23 (1.14 to 1.33)	

Statistical analyses

No statistical analyses for this end point

Primary: Specific image-based airway resistance (siRaw)

End point title	Specific image-based airway resistance (siRaw)[2]
End point description: Specific image-based airway resistance (siRaw). Average across lobes, adjusted for lobe volume. Ratio to baseline.	
End point type	Primary
End point timeframe: Day 15	

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: Data not available in compatible format to enter statistical analysis.

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: kPa·s				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.75 (0.59 to 0.95)	0.56 (0.44 to 0.71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Image-based airway volume (iVaw)

End point title	Image-based airway volume (iVaw)

End point description:

Image-based airway volume (iVaw) without correction for lobe volume. Ratio to baseline.

End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: mL				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	1.12 (1.01 to 1.24)	1.21 (1.12 to 1.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Image-based airway resistance (iRaw)

End point title	Image-based airway resistance (iRaw)

End point description:

Image-based airway resistance (iRaw) without correction for lobe volume. Ratio to baseline.

End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: kPa·s·L^-1				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.76 (0.59 to 0.97)	0.55 (0.41 to 0.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: FEV1

End point title	FEV1

End point description:

FEV1 Change from baseline in Forced Expiratory Volume at 1 second.

End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: Liters				
arithmetic mean (standard deviation)	999999999 (± 999999999)	0.065 (± 0.193)	0.151 (± 0.293)	

Statistical analyses

No statistical analyses for this end point

Secondary: Functional residual capacity (FRC)

End point title	Functional residual capacity (FRC)

End point description:

Functional residual capacity (FRC). Ratio to baseline.

End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GP MDI	FF MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: Liter				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.978 (0.891 to 1.073)	0.938 (0.833 to 1.056)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time the subject signed informed consent throughout the treatment period and up to 14 days following the last dose of study drug.

Adverse event reporting additional description:

The Safety Population was defined as all subjects who were randomized to treatment regardless and received at least one dose of study treatment. Serious adverse events collected from the time the subject signed consent up to 14 days following the last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	GP MDI

Reporting group description:

Glycopyrronium Metered Dose Inhalation

Reporting group title	FF MDI

Reporting group description:

FF MDI Formoterol Fumarate Metered Dose Inhalation

Serious adverse events	GP MDI	FF MDI	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	1 / 22 (4.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-Hodgkin's Lymphoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	GP MDI	FF MDI	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	3 / 22 (13.64%)	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 20 (5.00%)	3 / 22 (13.64%)	
occurrences (all)	1	3	
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 20 (10.00%)	1 / 22 (4.55%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2016	Change from single center to multi-center Minor updates/clarifications to study design Revised to provide clarification on which FEV1 values at Visit 4 will be used to assess stability criteria Revised to provide clarification on the duration of each treatment period (15 days ± 5 days) and when baseline will be obtained. Revised to provide clarification of the prohibited COPD medications and the wash-out requirements of prohibited COPD medications prior to Visit 1 (Screening)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported