Clinical trial results:
A PHASE 2B, RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ONCE-DAILY ORALLY ADMINISTERED PH-797804 FOR 12 WEEKS IN ADULTS WITH MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) ON A BACKGROUND OF TIOTROPIUM BROMIDE

Summary

EudraCT number	2011-005864-11
Trial protocol	CZ HU SE PL SK ES BG DE
Global end of trial date	18 September 2013

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	11 July 2015

Trial information

Trial identification

Sponsor protocol code	A6631033

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01543919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017, New York, United States, 10017
Public contact	Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	18 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2013
Global end of trial reached?	Yes
Global end of trial date	18 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the dose response relationship of PH-797804 on change from baseline in trough (pre-treatment and pre-bronchodilator) FEV1 at Week 12 compared to placebo in COPD patients on a background of tiotropium.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed; in particular, those affording greater protection to the safety of study subjects.

Background therapy:

Tiotropium bromide 18 microgram (mcg) once daily

Evidence for comparator: -

Actual start date of recruitment	13 April 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	Poland: 15
Country: Number of subjects enrolled	Slovakia: 94
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Sweden: 44
Country: Number of subjects enrolled	Bulgaria: 60
Country: Number of subjects enrolled	Czech Republic: 82
Country: Number of subjects enrolled	Germany: 68
Country: Number of subjects enrolled	Hungary: 99
Country: Number of subjects enrolled	Argentina: 12
Country: Number of subjects enrolled	Canada: 39
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	South Africa: 30
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 121
Worldwide total number of subjects	721
EEA total number of subjects	475

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)	385
From 65 to 84 years	336
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in 14 countries (Canada, United States, South Africa, Hungary, Argentina, Bulgaria, Czech Republic, Germany, Japan, Poland, Slovakia, Spain, Sweden, and Taiwan). Male or female subjects of 40 to 80 years inclusive, with a diagnosis, for at least 6 months, of moderate to severe COPD (GOLD) were enrolled.

Period 1

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

Blinding implementation details:

The study adopted a double-blind design to preserve the blinding. A double dummy system was utilized in order to maintain the blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo matched to PH-797804 tablet plus tiotropium bromide 18 microgram (mcg) orally once daily for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets matching the different doses of PH-797804 plus tiotropium bromide were administered orally once per day in the morning for 12 weeks.

Arm title	PH-797804 0.25 mg

Arm description:

Subjects received PH-797804 0.25 milligram (mg) plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	PH-797804 0.25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PH-797804 0.25 mg plus tiotropium bromide was administered orally once per day in the morning for 12 weeks.

Arm title	PH-797804 1 mg

Arm description:

Subjects received PH-797804 1 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	PH-797804
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PH-797804 1 mg plus tiotropium bromide was administered orally once per day in the morning for 12 weeks.

Arm title	PH-797804 3 mg

Arm description:

Subjects received PH-797804 3 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	PH-797804
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PH-797804 3 mg plus tiotropium bromide was administered orally once per day in the morning for 12 weeks.

Arm title	PH-797804 6 mg

Arm description:

Subjects received PH-797804 6 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	PH-797804
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PH-797804 6 mg plus tiotropium bromide was administered orally once per day in the morning for 12 weeks.

Arm title	PH-797804 10 mg

Arm description:

Subjects received PH-797804 10 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	PH-797804
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PH-797804 10 mg plus tiotropium bromide was administered orally once per day in the morning for 12 weeks.

Number of subjects in period 1	Placebo	PH-797804 0.25 mg	PH-797804 1 mg
Started	181	90	91
Treated/Baseline	181	90	91
Completed	162	79	76
Not completed	19	11	15
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	2	1	2
Did not meet entrance criteria	4	1	1
Adverse event, non-fatal	9	8	7
Unspecified	1	1	3
Insufficient clinical response	1	-	1
Protocol deviation	-	-	1

Number of subjects in period 1	PH-797804 3 mg	PH-797804 6 mg	PH-797804 10 mg
Started	88	182	89
Treated/Baseline	88	182	89
Completed	75	153	70
Not completed	13	29	19
Adverse event, serious fatal	-	2	-
Consent withdrawn by subject	1	4	1
Did not meet entrance criteria	1	2	3
Adverse event, non-fatal	11	19	14
Unspecified	-	-	1
Insufficient clinical response	-	-	-
Protocol deviation	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to PH-797804 tablet plus tiotropium bromide 18 microgram (mcg) orally once daily for 12 weeks.	
Reporting group title	PH-797804 0.25 mg
Reporting group description:	
Subjects received PH-797804 0.25 milligram (mg) plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 1 mg
Reporting group description:	
Subjects received PH-797804 1 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 3 mg
Reporting group description:	
Subjects received PH-797804 3 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 6 mg
Reporting group description:	
Subjects received PH-797804 6 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 10 mg
Reporting group description:	
Subjects received PH-797804 10 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	

Reporting group values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg
Number of subjects	181	90	91
Age categorical Units: Subjects			
18 to 44 years	1	0	1
45 to 64 years	103	52	51
Greater than or equal to (>=) 65 years	77	38	39
Gender categorical Units: Subjects			
Female	60	33	38
Male	121	57	53

Reporting group values	PH-797804 3 mg	PH-797804 6 mg	PH-797804 10 mg
Number of subjects	88	182	89
Age categorical Units: Subjects			
18 to 44 years	0	2	1
45 to 64 years	49	92	33
Greater than or equal to (>=) 65 years	39	88	55
Gender categorical Units: Subjects			
Female	33	67	37
Male	55	115	52

Reporting group values	Total		
Number of subjects	721		
Age categorical Units: Subjects			
18 to 44 years	5		
45 to 64 years	380		
Greater than or equal to (>=) 65 years	336		
Gender categorical Units: Subjects			
Female	268		
Male	453		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to PH-797804 tablet plus tiotropium bromide 18 microgram (mcg) orally once daily for 12 weeks.	
Reporting group title	PH-797804 0.25 mg
Reporting group description:	
Subjects received PH-797804 0.25 milligram (mg) plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 1 mg
Reporting group description:	
Subjects received PH-797804 1 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 3 mg
Reporting group description:	
Subjects received PH-797804 3 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 6 mg
Reporting group description:	
Subjects received PH-797804 6 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	
Reporting group title	PH-797804 10 mg
Reporting group description:	
Subjects received PH-797804 10 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.	

Primary: Placebo-corrected change from baseline in trough (pre-treatment and pre-bronchodilator) FEV1 at Week 12

End point title	Placebo-corrected change from baseline in trough (pre-treatment and pre-bronchodilator) FEV1 at Week 12[1][2]
End point description:	
Forced expiratory volume in 1 second (FEV1) is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Trough FEV1 was obtained from spirometry, performed before study treatment administration. The primary objective of the study was to characterize the dose-response relationship of PH-797804 on change from baseline in trough (pre-treatment and pre-bronchodilator) FEV1 at Week 12 compared to placebo in subjects with COPD on a background of tiotropium. The dose-response relationship of change from baseline trough FEV1 at Week 12 was modeled using a Bayesian maximum possible effect (Emax) model. Placebo-adjusted data was reported. Analysis was done on the Per-Protocol Analysis Set (PPAS) which consisted of all subjects who had no major protocol violations and produced valid trough FEV1 readings at both baseline and the Week 12 visit.	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

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: A Bayesian maximum possible effect (Emax) model with weakly informative priors was employed to test if any of the doses were efficacious compared to placebo based on predefined decision criteria. However, none of the 5 doses of PH-797804 met the predefined decision criteria for improvement over placebo in change from baseline trough FEV1 at Week 12.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-corrected estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	86	86	172
Units: Liter (L)				
number (confidence interval 95%)	0.0316 (0.00209 to 0.0717)	0.0472 (0.00703 to 0.0877)	0.0554 (0.0145 to 0.0949)	0.0587 (0.0184 to 0.0982)

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Liter (L)				
number (confidence interval 95%)	0.0604 (0.0202 to 0.0999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in trough, pre-bronchodilator FEV1 at Weeks 2, 6, and 10

End point title	Placebo-adjusted change from baseline in trough, pre-bronchodilator FEV1 at Weeks 2, 6, and 10[3]

End point description:

FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Trough FEV1 was obtained from spirometry, performed before study treatment administration. The change from baseline in trough, pre-bronchodilator FEV1 at Weeks 2, 6, and 10 was analyzed using a longitudinal mixed effects model with treatment, week and treatment-by-week interaction fitted as factors, and the baseline value as a covariate. Placebo-adjusted data was reported. Analysis was done on the Full Analysis Set (FAS) which included all randomized subjects, who had at least 1 valid FEV1 measurement during the active double-blind phase of the study. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, and 10

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[4]	88[5]	86[6]	175[7]
Units: Liter (L)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0488 (± 0.0197)	0.0723 (± 0.0201)	0.0658 (± 0.0201)	0.0695 (± 0.0162)

Week 6 (n=84, 78, 78, 158, 78)	0.0469 (± 0.241)	0.0648 (± 0.0247)	0.0301 (± 0.0247)	0.0532 (± 0.02)
Week 10 (n=80, 74, 77, 147, 70)	0.0501 (± 0.0261)	0.0612 (± 0.0267)	0.0225 (± 0.0265)	0.0503 (± 0.0217)

Notes:

[4] - Subjects who were evaluable for this measure.

[5] - Subjects who were evaluable for this measure.

[6] - Subjects who were evaluable for this measure.

[7] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[8]			
Units: Liter (L)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0567 (± 0.02)			
Week 6 (n=84, 78, 78, 158, 78)	0.0668 (± 0.0247)			
Week 10 (n=80, 74, 77, 147, 70)	0.0355 (± 0.027)			

Notes:

[8] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in trough, pre-bronchodilator forced expiratory volume in 6 seconds (FEV6) at Weeks 2, 6, 10 and 12

End point title	Placebo-adjusted change from baseline in trough, pre-bronchodilator forced expiratory volume in 6 seconds (FEV6) at Weeks 2, 6, 10 and 12[9]

End point description:

FEV6 is the maximal volume of air exhaled in the first 6 seconds of a forced expiration from a position of full inspiration. Trough FEV6 was obtained from spirometry, performed before study treatment administration. The change from baseline in trough, pre-bronchodilator FEV6 at Weeks 2, 6, 10 and 12 was analyzed using a longitudinal mixed effects model with treatment, week and treatment-by-week interaction fitted as factors, and the baseline value as a covariate. Placebo-adjusted data was reported. Analysis was done on the FAS population which included all randomized subjects, who had at least 1 valid FEV1 measurement during the active double-blind phase of the study. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[10]	88[11]	86[12]	175[13]
Units: Liter (L)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0523 (± 0.0266)	0.0806 (± 0.0272)	0.0439 (± 0.0271)	0.0707 (± 0.0219)
Week 6 (n=84, 78, 78, 158, 78)	0.0643 (± 0.0338)	0.075 (± 0.0346)	-0.0003 (± 0.0345)	0.0365 (± 0.028)
Week 10 (n=80, 74, 77, 147, 70)	0.0591 (± 0.0337)	0.0556 (± 0.0346)	-0.0037 (± 0.0343)	0.0427 (± 0.0281)
Week 12 (n=78, 73, 73, 146, 69)	0.0351 (± 0.036)	0.1132 (± 0.0368)	0.0119 (± 0.0367)	0.0367 (± 0.0298)

Notes:

[10] - Subjects who were evaluable for this measure.

[11] - Subjects who were evaluable for this measure.

[12] - Subjects who were evaluable for this measure.

[13] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[14]			
Units: Liter (L)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0558 (± 0.027)			
Week 6 (n=84, 78, 78, 158, 78)	0.0817 (± 0.0346)			
Week 10 (n=80, 74, 77, 147, 70)	0.0366 (± 0.035)			
Week 12 (n=78, 73, 73, 146, 69)	0.0347 (± 0.0373)			

Notes:

[14] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in trough, pre-bronchodilator forced vital capacity (FVC) at Weeks 2, 6, 10 and 12

End point title	Placebo-adjusted change from baseline in trough, pre-bronchodilator forced vital capacity (FVC) at Weeks 2, 6, 10 and 12[15]

End point description:

FVC is the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Trough FVC was obtained from spirometry, performed before study treatment administration. The change from baseline in trough, pre-bronchodilator FVC at Weeks 2, 6, 10 and 12 was analyzed using a longitudinal mixed effects model with treatment, week and treatment-by-week interaction fitted as factors, and the baseline value as a covariate. Placebo-adjusted data was reported. Analysis was done on the FAS population which included all randomized subjects, who had at least 1 valid FEV1 measurement during the active double-blind phase of the study."n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[16]	88[17]	86[18]	175[19]
Units: litre(s)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0595 (± 0.032)	0.058 (± 0.0328)	0.0054 (± 0.0327)	0.0686 (± 0.0264)
Week 6 (n=84, 78, 78, 158, 78)	0.0647 (± 0.0419)	0.0511 (± 0.043)	-0.0401 (± 0.0429)	0.003 (± 0.0348)
Week 10 (n=80, 74, 77, 147, 70)	0.0479 (± 0.0406)	0.0398 (± 0.0416)	-0.0575 (± 0.0412)	0.0153 (± 0.0338)
Week 12 (n=78, 73, 73, 146, 69)	0.0214 (± 0.0431)	0.0907 (± 0.0441)	-0.0295 (± 0.044)	0.0026 (± 0.0357)

Notes:

[16] - Subjects who were evaluable for this measure.

[17] - Subjects who were evaluable for this measure.

[18] - Subjects who were evaluable for this measure.

[19] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[20]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 2 (n=88, 82, 83, 171, 84)	0.0447 (± 0.0326)			
Week 6 (n=84, 78, 78, 158, 78)	0.0665 (± 0.043)			
Week 10 (n=80, 74, 77, 147, 70)	0.0235 (± 0.0421)			
Week 12 (n=78, 73, 73, 146, 69)	0.0295 (± 0.0446)			

Notes:

[20] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in trough, pre-bronchodilator inspiratory capacity (IC) at Weeks 2, 6, 10 and 12

End point title	Placebo-adjusted change from baseline in trough, pre-bronchodilator inspiratory capacity (IC) at Weeks 2, 6, 10 and 12[21]

End point description:

IC is the maximum volume of air that can be inhaled into the lungs from the normal resting position

after breathing out
normally. Trough IC was obtained from spirometry, performed before study treatment administration. The change from baseline
in trough, pre-bronchodilator IC at Weeks 2, 6, 10 and 12 was analyzed using a longitudinal mixed effects model with treatment,
week and treatment-by-week interaction fitted as factors, and the baseline value as a covariate. Placebo-adjusted data was
reported. Analysis was done on the FAS which included all randomized subjects, who had at least 1 valid FEV1 measurement during the active double-blind phase of the study. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[22]	88[23]	86[24]	175[25]
Units: litre(s)				
arithmetic mean (standard error)				
Week 2 (n=88, 83, 83, 171, 85)	0.0151 (± 0.0384)	0.0596 (± 0.0392)	0.0905 (± 0.0392)	0.0704 (± 0.0316)
Week 6 (n=84, 78, 78, 158, 77)	0.0758 (± 0.0422)	0.0721 (± 0.0433)	0.0277 (± 0.0432)	0.0607 (± 0.035)
Week 10 (n=80, 74, 77, 147, 70)	-0.0065 (± 0.0437)	0.0133 (± 0.0449)	0.0202 (± 0.0444)	0.0099 (± 0.0364)
Week 12 (n=78, 73, 73, 146, 69)	-0.0671 (± 0.0441)	0.0745 (± 0.0451)	0.0661 (± 0.0451)	0.0179 (± 0.0366)

Notes:

[22] - Subjects who were evaluable for this measure.

[23] - Subjects who were evaluable for this measure.

[24] - Subjects who were evaluable for this measure.

[25] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[26]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 2 (n=88, 83, 83, 171, 85)	0.0762 (± 0.0389)			
Week 6 (n=84, 78, 78, 158, 77)	0.0428 (± 0.0433)			
Week 10 (n=80, 74, 77, 147, 70)	0.0429 (± 0.0455)			
Week 12 (n=78, 73, 73, 146, 69)	0.0419 (± 0.0457)			

Notes:

[26] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Average placebo-adjusted change from baseline in trough, pre-bronchodilator FEV1, FEV6, FVC, and IC over 12 weeks of treatment

End point title	Average placebo-adjusted change from baseline in trough, pre-bronchodilator FEV1, FEV6, FVC, and IC over 12 weeks of treatment[27]

End point description:

FEV1=the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration; FEV6=the
maximal volume of air exhaled in the first 6 seconds of a forced expiration from a position of full inspiration; FVC=the volume of
air which can be forcibly exhaled from the lungs after taking the deepest breath possible; IC=the maximum volume of air that
can be inhaled into the lungs from the normal resting position after breathing out normally. Trough FEV1, FEV6, FVC, and IC
were obtained from spirometry, performed before study treatment administration. The average change from baseline in trough,
pre-bronchodilator FEV1, FEV6, FVC, and IC over 12 weeks of treatment was analyzed using a longitudinal mixed effects model
with treatment, week and treatment-by-week interaction fitted as factors, and the baseline value as a covariate. Placebo-adjusted
data was reported. "n" signifies subjects with available data for each arm respectively. FAS used.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[28]	88[29]	86[30]	175[31]
Units: litre(s)				
arithmetic mean (standard error)				
FEV1 (n=88, 83, 83, 172, 84)	0.0455 (± 0.0194)	0.0745 (± 0.0198)	0.0397 (± 0.0198)	0.0563 (± 0.0161)
FEV6 (n=88,83, 83, 172, 84)	0.0527 (± 0.0259)	0.0811 (± 0.0265)	0.013 (± 0.0264)	0.0467 (± 0.0214)
FVC (n=88, 83, 83, 172, 84)	0.0484 (± 0.0318)	0.0599 (± 0.0325)	-0.0304 (± 0.0324)	0.0224 (± 0.0263)
IC (n=88, 83, 83, 172, 85)	0.0043 (± 0.0327)	0.0549 (± 0.0334)	0.0511 (± 0.0333)	0.0397 (± 0.0271)

Notes:

[28] - Subjects who were evaluable for this measure.

[29] - Subjects who were evaluable for this measure.

[30] - Subjects who were evaluable for this measure.

[31] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[32]			
Units: litre(s)				
arithmetic mean (standard error)				

FEV1 (n=88, 83, 83, 172, 84)	0.052 (± 0.0199)			
FEV6 (n=88,83, 83, 172, 84)	0.0522 (± 0.0266)			
FVC (n=88, 83, 83, 172, 84)	0.041 (± 0.0326)			
IC (n=88, 83, 83, 172, 85)	0.0509 (± 0.0335)			

Notes:

[32] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FEV1 at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FEV1 at Weeks 0 and 12[33]

End point description:

FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Trough
FEV1 was obtained from spirometry, performed before study treatment administration. The change from baseline in post-study
drug, pre-bronchodilator FEV1 at Weeks 0 and 12 was analyzed using the analyis of covariance (ANCOVA) model with treatment
as a fixed effect and baseline value as a covariate. Post-study drug spirometry was performed 15-30 minutes after administration
of study drug at the Weeks 0 and 12 visits. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[34]	88[35]	86[36]	175[37]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	0.0026 (± 0.013)	-0.0011 (± 0.0132)	0.0052 (± 0.0132)	0.0128 (± 0.0107)
Week 12 (n=77, 72, 72, 146, 69)	-0.011 (± 0.0116)	-0.0121 (± 0.0119)	-0.0137 (± 0.0119)	-0.0064 (± 0.0096)

Notes:

[34] - Subjects who were evaluable for this measure.

[35] - Subjects who were evaluable for this measure.

[36] - Subjects who were evaluable for this measure.

[37] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			

Subject group type	Reporting group			
Number of subjects analysed	88[38]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	-0.0019 (± 0.0131)			
Week 12 (n=77, 72, 72, 146, 69)	0.0045 (± 0.0121)			

Notes:

[38] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FEV6 at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FEV6 at Weeks 0 and 12[39]

End point description:

FEV6 is the maximal volume of air exhaled in the first 6 seconds of a forced expiration from a position of full inspiration.
Trough FEV6 was obtained from spirometry, performed before study treatment administration. The change from baseline in
post-study drug, pre-bronchodilator FEV6 at Weeks 0 and 12 was analyzed using the ANCOVA model with treatment as a
fixed effect and baseline value as a covariate. Post-study drug spirometry was performed 15-30 minutes after administration
of study drug at the Weeks 0 and 12 visits. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[40]	88[41]	86[42]	175[43]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	0.0239 (± 0.0188)	0.0046 (± 0.0192)	-0.0061 (± 0.0191)	0.0176 (± 0.0155)
Week 12 (n=77, 72, 72, 146, 69)	-0.0163 (± 0.0168)	-0.0095 (± 0.0172)	-0.0226 (± 0.0172)	-0.0115 (± 0.0139)

Notes:

[40] - Subjects who were evaluable for this measure.

[41] - Subjects who were evaluable for this measure.

[42] - Subjects who were evaluable for this measure.

[43] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			

Subject group type	Reporting group			
Number of subjects analysed	88[44]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	0.0009 (± 0.019)			
Week 12 (n=77, 72, 72, 146, 69)	-0.0095 (± 0.0175)			

Notes:

[44] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator IC at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator IC at Weeks 0 and 12[45]

End point description:

IC is the maximum volume of air that can be inhaled into the lungs from the normal resting position after breathing out
normally. Trough IC was obtained from spirometry, performed before study treatment administration. The change from
baseline in post-study drug, pre-bronchodilator IC at Weeks 0 and 12 was analyzed using the ANCOVA model with
treatment as a fixed effect and baseline value as a covariate. Post-study drug spirometry was performed 15-30 minutes
after administration of study drug at the Weeks 0 and 12 visits. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[46]	88[47]	86[48]	175[49]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	-0.0577 (± 0.0353)	-0.1135 (± 0.0358)	-0.0957 (± 0.0358)	-0.0768 (± 0.029)
Week 12 (n=77, 72, 73, 146, 69)	0.0555 (± 0.0321)	0.0092 (± 0.0328)	-0.0075 (± 0.0327)	0.0203 (± 0.0265)

Notes:

[46] - Subjects who were evaluable for this measure.

[47] - Subjects who were evaluable for this measure.

[48] - Subjects who were evaluable for this measure.

[49] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[50]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	-0.0759 (± 0.0356)			
Week 12 (n=77, 72, 73, 146, 69)	-0.0116 (± 0.0333)			

Notes:

[50] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FEV1 at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FEV1 at Weeks 0 and 12[51]

End point description:

FEV1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. Trough
FEV1 was obtained from spirometry, performed before study treatment administration. The change from baseline in poststudy
drug, post-bronchodilator FEV1 at Weeks 0 and 12 was analyzed using the ANCOVA model with treatment as a fixed
effect and baseline value as a covariate. Post-bronchodilator spirometry measurements were performed 15-30 minutes after
the administration of salbutamol (albuterol) 400 mcg via a metered dose inhaler (MDI) (spacer, where available). Placeboadjusted
data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[52]	88[53]	86[54]	175[55]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	0.0023 (± 0.0187)	0.0143 (± 0.019)	-0.0014 (± 0.019)	-0.0022 (± 0.0154)
Week 12 (n=76, 72, 71, 143, 69)	-0.0017 (± 0.0286)	0.0626 (± 0.0292)	0.0179 (± 0.0293)	0.0121 (± 0.0237)

Notes:

[52] - Subjects who were evaluable for this measure.

[53] - Subjects who were evaluable for this measure.

[54] - Subjects who were evaluable for this measure.

[55] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[56]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	-0.0153 (± 0.0189)			
Week 12 (n=76, 72, 71, 143, 69)	0.025 (± 0.0296)			

Notes:

[56] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FEV6 at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FEV6 at Weeks 0 and 12[57]

End point description:

FEV6 is the maximal volume of air exhaled in the first 6 seconds of a forced expiration from a position of full inspiration.
Trough FEV6 was obtained from spirometry, performed before study treatment administration. The change from baseline in
post-study drug, post-bronchodilator FEV6 at Weeks 0 and 12 was analyzed using the ANCOVA model with treatment as a
fixed effect and baseline value as a covariate. Post-bronchodilator spirometry measurements were performed 15-30 minutes
after the administration of salbutamol (albuterol) 400 mcg via an MDI (spacer, where available). Placebo-adjusted data was
reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[58]	88[59]	86[60]	175[61]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	-0.0019 (± 0.0253)	0.0082 (± 0.0257)	-0.0025 (± 0.0258)	-0.0014 (± 0.0208)
Week 12 (n=76, 72, 71, 143, 69)	0.0007 (± 0.0376)	0.0576 (± 0.0383)	0.0049 (± 0.0385)	0.0088 (± 0.0311)

Notes:

[58] - Subjects who were evaluable for this measure.

[59] - Subjects who were evaluable for this measure.

[60] - Subjects who were evaluable for this measure.

[61] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[62]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	-0.001 (± 0.0256)			
Week 12 (n=76, 72, 71, 143, 69)	0.0173 (± 0.0389)			

Notes:

[62] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FVC at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, post-bronchodilator FVC at Weeks 0 and 12[63]

End point description:

FVC is the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Trough FVC
was obtained from spirometry, performed before study treatment administration. The change from baseline in post-study
drug, post-bronchodilator FVC at Weeks 0 and 12 was analyzed using the ANCOVA model with treatment as a fixed effect
and baseline value as a covariate. Post-bronchodilator spirometry measurements were performed 15-30 minutes after the
administration of salbutamol (albuterol) 400 mcg via an MDI (spacer, where available). Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[64]	88[65]	86[66]	175[67]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	0.03 (± 0.0335)	0.0203 (± 0.0341)	-0.0048 (± 0.0342)	0.0204 (± 0.0276)

Week 12 (n=76, 72, 71, 143, 69)	0.005 (± 0.0441)	0.0517 (± 0.045)	-0.0044 (± 0.0452)	0.0076 (± 0.0365)

Notes:

[64] - Subjects who were evaluable for this measure.

[65] - Subjects who were evaluable for this measure.

[66] - Subjects who were evaluable for this measure.

[67] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[68]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 86)	0.0194 (± 0.0339)			
Week 12 (n=76, 72, 71, 143, 69)	0.0242 (± 0.0457)			

Notes:

[68] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, post-bronchodilator IC at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, post-bronchodilator IC at Weeks 0 and 12[69]

End point description:

IC is the maximum volume of air that can be inhaled into the lungs from the normal resting position after breathing out
normally. Trough IC was obtained from spirometry, performed before study treatment administration. The change from
baseline in post-study drug, post-bronchodilator IC at Weeks 0 and 12 was analyzed using the ANCOVA model with
treatment as a fixed effect and baseline value as a covariate. Post-bronchodilator spirometry measurements were performed
15-30 minutes after the administration of salbutamol (albuterol) 400 mcg via an MDI (spacer, where available). Placebo-adjusted
data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[70]	88[71]	86[72]	175[73]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 87)	0.0284 (± 0.038)	-0.0025 (± 0.0386)	-0.0679 (± 0.0387)	-0.0249 (± 0.0313)
Week 12 (n=76, 72, 72, 144, 69)	0.0341 (± 0.0497)	0.0071 (± 0.0506)	-0.0187 (± 0.0506)	-0.0345 (± 0.041)

Notes:

[70] - Subjects who were evaluable for this measure.

[71] - Subjects who were evaluable for this measure.

[72] - Subjects who were evaluable for this measure.

[73] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[74]			
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 84, 173, 87)	-0.0624 (± 0.0383)			
Week 12 (n=76, 72, 72, 144, 69)	-0.0014 (± 0.0514)			

Notes:

[74] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in chronic obstructive pulmonary disease (COPD) symptoms using The EXAcerbations of Chronic Pulmonary Disease Tool (EXACT) Respiratory Symptom (E-RS) Diary over 12 weeks of treatment

End point title	Placebo-adjusted change from baseline in chronic obstructive pulmonary disease (COPD) symptoms using The EXAcerbations of Chronic Pulmonary Disease Tool (EXACT) Respiratory Symptom (E-RS) Diary over 12 weeks of treatment[75]

End point description:

Subjects were required to evaluate the severity of their respiratory symptoms on a daily basis in the evening using an electronic diary by rating their respiratory symptoms according to how they felt during the preceding 24 hours (including the previous night). The E-RS was part of the EXACT and consisted of 11 out of 14 items relating to the 3 domains of breathlessness, cough and sputum, and chest symptoms. Each question (item) was summed to yield a total score which was converted to an EXACT total score on a 0 to 100 scale. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data for each score in each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[76]	88[77]	86[78]	175[79]
Units: units on a scale				
arithmetic mean (standard error)				
Breathlessness score (n=89, 87, 86, 173, 88)	0.0079 (± 0.2149)	-0.1272 (± 0.2177)	0.1058 (± 0.2183)	0.117 (± 0.1772)
Cough & sputum score (n=89, 87, 86, 173, 88)	0.0323 (± 0.1208)	-0.1372 (± 0.1227)	-0.1408 (± 0.1229)	-0.1029 (± 0.0997)
Chest symptoms score (n=89, 87, 86, 173, 88)	-0.0549 (± 0.1375)	-0.1434 (± 0.1395)	0.0615 (± 0.1398)	-0.0181 (± 0.1135)
Total score (n=89, 87, 86, 173, 88)	-0.0326 (± 0.4177)	-0.3896 (± 0.4234)	0.0266 (± 0.4244)	-0.003 (± 0.3447)

Notes:

[76] - Subjects who were evaluable for this measure.

[77] - Subjects who were evaluable for this measure.

[78] - Subjects who were evaluable for this measure.

[79] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[80]			
Units: units on a scale				
arithmetic mean (standard error)				
Breathlessness score (n=89, 87, 86, 173, 88)	-0.0445 (± 0.2175)			
Cough & sputum score (n=89, 87, 86, 173, 88)	-0.307 (± 0.1225)			
Chest symptoms score (n=89, 87, 86, 173, 88)	-0.0599 (± 0.1393)			
Total score (n=89, 87, 86, 173, 88)	-0.4013 (± 0.4228)			

Notes:

[80] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in Chronic Respiratory Questionnaire - Self Administered Standard (CRQ-SAS) at Weeks 2, 6, 10 and 12 - Dyspnea domain

End point title	Placebo-adjusted change from baseline in Chronic Respiratory Questionnaire - Self Administered Standard (CRQ-SAS) at Weeks 2, 6, 10 and 12 - Dyspnea domain[81]

End point description:

The CRQ-SAS questionnaire is a COPD specific measure of quality of life. It includes 20 items measuring 4 domains: Dyspnea
(5 items), Fatigue (4 items), Emotional Function (7 Items), and Mastery (4 items). Subjects were asked

to record their
answers on a 7-point scale (1 = maximum impairment to 7 = no impairment). The scores for each question of each domain
were simply added together and divided by the number of questions in the domain. Due to the scaling of the responses on
the CRQ-SAS, an increase in scoring from baseline would show a therapeutic benefit of the medication. Dyspnea domain
score ranged from 1 to 7, where higher score indicated lesser impairment. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, no data for placebo can be obtained.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[82]	88[83]	86[84]	175[85]
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=80, 74, 79, 158, 74)	0.0434 (± 0.1013)	0.0114 (± 0.1042)	0.0184 (± 0.102)	-0.0277 (± 0.0828)
Week 6 (n=77, 66, 74, 148, 70)	0.1235 (± 0.1122)	0.0382 (± 0.117)	0.0381 (± 0.1138)	0.0167 (± 0.0922)
Week 10 (n-73, 65, 72, 136, 59)	0.0764 (± 0.1196)	0.0364 (± 0.1239)	-0.1663 (± 0.1206)	-0.0454 (± 0.0986)
Week 12 (n=72, 63, 67, 139, 61)	-0.0227 (± 0.1259)	-0.0504 (± 0.131)	-0.0171 (± 0.1282)	-0.0586 (± 0.1034)

Notes:

[82] - Subjects who were evaluable for this measure.

[83] - Subjects who were evaluable for this measure.

[84] - Subjects who were evaluable for this measure.

[85] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[86]			
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=80, 74, 79, 158, 74)	-0.1151 (± 0.1036)			
Week 6 (n=77, 66, 74, 148, 70)	-0.0685 (± 0.1152)			
Week 10 (n-73, 65, 72, 136, 59)	-0.1943 (± 0.1257)			
Week 12 (n=72, 63, 67, 139, 61)	0.0261 (± 0.1316)			

Notes:

[86] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Fatigue domain

End point title	Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Fatigue domain[87]

End point description:

The CRQ-SAS questionnaire is a COPD specific measure of quality of life. It includes 20 items measuring 4 domains: Dyspnea
(5 items), Fatigue (4 items), Emotional Function (7 Items), and Mastery (4 items). Subjects were asked to record their
answers on a 7-point scale (1 = maximum impairment to 7 = no impairment). The scores for each question of each domain
were simply added together and divided by the number of questions in the domain. An increase in scoring from baseline
would show a therapeutic benefit of the medication. Fatigue domain score ranged from 1 to 7, where higher score indicated less impairment. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[88]	88[89]	86[90]	175[91]
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	0.0162 (± 0.0891)	0.068 (± 0.0906)	0.04 (± 0.0906)	-0.086 (± 0.0733)
Week 6 (n=83, 78, 80, 158, 79)	0.0224 (± 0.1073)	0.0358 (± 0.1094)	-0.0018 (± 0.1087)	-0.0891 (± 0.0887)
Week 10 (n=79, 73, 76, 147, 70)	-0.0355 (± 0.1088)	0.0362 (± 0.1114)	-0.157 (± 0.1102)	-0.134 (± 0.0902)
Week 12 (n=78, 73, 74, 147, 69)	-0.0448 (± 0.1157)	0.0199 (± 0.1182)	-0.0368 (± 0.1175)	-0.136 (± 0.0958)

Notes:

[88] - Subjects who were evaluable for this measure.

[89] - Subjects who were evaluable for this measure.

[90] - Subjects who were evaluable for this measure.

[91] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[92]			
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	-0.0199 (± 0.0905)			
Week 6 (n=83, 78, 80, 158, 79)	-0.0155 (± 0.1089)			

Week 10 (n=79, 73, 76, 147, 70)	-0.0726 (± 0.1123)			
Week 12 (n=78, 73, 74, 147, 69)	-0.0037 (± 0.1196)			

Notes:

[92] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Emotional Function domain

End point title	Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Emotional Function domain[93]

End point description:

The CRQ-SAS questionnaire is a COPD specific measure of quality of life. It includes 20 items measuring 4 domains: Dyspnea
(5 items), Fatigue (4 items), Emotional Function (7 Items), and Mastery (4 items). Subjects were asked to record their
answers on a 7-point scale (1 = maximum impairment to 7 = no impairment). The scores for each question of each domain
were simply added together and divided by the number of questions in the domain. An increase in scoring from baseline
would show a therapeutic benefit of the medication. Emotional function domain score ranged from 1 to 7, where higher
score indicated lesser impairment. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[93] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[94]	88[95]	86[96]	175[97]
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	0.0532 (± 0.0796)	0.0655 (± 0.0812)	0.0268 (± 0.0809)	-0.0247 (± 0.0654)
Week 6 (n=83, 78, 80, 158, 79)	0.0617 (± 0.0964)	-0.0007 (± 0.0985)	-0.0927 (± 0.0976)	-0.0592 (± 0.0796)
Week 10 (n=79, 74, 77, 147, 70)	-0.0633 (± 0.0974)	-0.0461 (± 0.0996)	-0.1031 (± 0.0984)	-0.1441 (± 0.0806)
Week 12 (n=78, 73, 74, 147, 69)	-0.0792 (± 0.1038)	-0.0561 (± 0.1062)	-0.1004 (± 0.1053)	-0.1281 (± 0.0859)

Notes:

[94] - Subjects who were evaluable for this measure.

[95] - Subjects who were evaluable for this measure.

[96] - Subjects who were evaluable for this measure.

[97] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[98]			
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	-0.0184 (± 0.0808)			
Week 6 (n=83, 78, 80, 158, 79)	-0.0063 (± 0.0978)			
Week 10 (n=79, 74, 77, 147, 70)	-0.1314 (± 0.1005)			
Week 12 (n=78, 73, 74, 147, 69)	-0.035 (± 0.1072)			

Notes:

[98] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Mastery domain

End point title	Placebo-adjusted change from baseline in CRQ-SAS at Weeks 2, 6, 10 and 12 - Mastery domain[99]

End point description:

The CRQ-SAS questionnaire is a COPD specific measure of quality of life. It includes 20 items measuring 4 domains: Dyspnea
(5 items), Fatigue (4 items), Emotional Function (7 Items), and Mastery (4 items). Subjects were asked to record their
answers on a 7-point scale (1 = maximum impairment to 7 = no impairment). The scores for each question of each domain
were simply added together and divided by the number of questions in the domain. An increase in scoring from baseline
would show a therapeutic benefit of the medication. Mastery domain score ranged from 1 to 7, where higher score indicated
lesser impairment. Placebo-adjusted data was reported. Analysis was done on the FAS. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10 and 12.

Notes:

[99] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[100]	88[101]	86[102]	175[103]
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	0.1131 (± 0.0996)	0.1527 (± 0.1014)	-0.0314 (± 0.1012)	0.0418 (± 0.0818)
Week 6 (n=83, 78, 80, 158, 79)	-0.027 (± 0.1123)	0.0832 (± 0.1146)	-0.0823 (± 0.1138)	-0.0822 (± 0.0927)

Week 10 (n=79, 73, 76, 147, 70)	-0.0142 (± 0.1156)	-0.1039 (± 0.1184)	-0.3125 (± 0.1171)	-0.0777 (± 0.0957)
Week 12 (n=78, 73, 74, 147, 69)	-0.1963 (± 0.1235)	-0.0387 (± 0.1263)	-0.3888 (± 0.1254)	-0.2103 (± 0.1021)

Notes:

[100] - Subjects who were evaluable for this measure.

[101] - Subjects who were evaluable for this measure.

[102] - Subjects who were evaluable for this measure.

[103] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[104]			
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=87, 83, 83, 171, 83)	0.0242 (± 0.1011)			
Week 6 (n=83, 78, 80, 158, 79)	-0.0767 (± 0.114)			
Week 10 (n=79, 73, 76, 147, 70)	-0.1277 (± 0.1192)			
Week 12 (n=78, 73, 74, 147, 69)	-0.2243 (± 0.1275)			

Notes:

[104] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of responses in the Patient Global Impression of Change at Week 12

End point title	Frequency of responses in the Patient Global Impression of Change at Week 12

End point description:

The subject's overall subjective rating of any change in their COPD symptoms since the start of the study was captured
in the Patient Global Impression of Change which was completed by subjects at Week 12. Responses consisted of very
much improved, much improved, minimally improved, no change, minimally worse, much worse, and very much worse. The
percentage of subjects with response based on the Patient Global Impression of Change were presented. All subjects in the FAS who had available data for this endpoint were included in this summary.

End point type	Secondary

End point timeframe:

Week 12.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	158	79	73	74
Units: Percentage of subjects				
number (not applicable)				
Very much improved	4.4	7.6	0	2.7
Much improved	12.7	17.7	23.3	21.6
Minimally improved	48.1	36.7	42.5	29.7
No change	31.6	32.9	31.5	33.8
Minimally worse	3.2	2.5	1.4	10.8
Much worse	0	2.5	1.4	1.4
Very much worse	0	0	0	0

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	69		
Units: Percentage of subjects				
number (not applicable)				
Very much improved	2.7	4.3		
Much improved	21.1	23.2		
Minimally improved	36.1	42		
No change	31.3	27.5		
Minimally worse	6.8	2.9		
Much worse	2	0		
Very much worse	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of responses in the Clinician Global Impression of Change at Week 12

End point title	Frequency of responses in the Clinician Global Impression of Change at Week 12

End point description:

The investigator’s overall rating of the change in the subject's COPD symptoms since the start of the study was captured
in the Clinician Global Impression of Change which was completed by the investigator at Week 12. Responses consisted of
very much improved, much improved, minimally improved, no change, minimally worse, much worse, and very much worse.
The percentage of subjects with response based on Clinician Global Impression of Change were presented. All subjects in the FAS who had available data for this endpoint were included in this summary.

End point type	Secondary

End point timeframe:

Week 12.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	157	78	73	74
Units: Percentage of subjects				
number (not applicable)				
Very much improved	2.5	1.3	0	5.4
Much improved	14.6	21.8	21.9	18.9
Minimally improved	44.6	39.7	34.2	27
No change	36.3	34.6	38.4	37.8
Minimally worse	1.9	2.6	5.5	9.5
Much worse	0	0	0	1.4
Very much worse	0	0	0	0

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	69		
Units: Percentage of subjects				
number (not applicable)				
Very much improved	4.1	4.3		
Much improved	18.6	13		
Minimally improved	36.6	37.7		
No change	31	42		
Minimally worse	9	2.9		
Much worse	0.7	0		
Very much worse	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted ratio in number of weekly puffs of rescue bronchodilator use (per daily diary)

End point title	Placebo-adjusted ratio in number of weekly puffs of rescue bronchodilator use (per daily diary)[105]

End point description:

Subjects recorded in the daily diary the total number of puffs of any short acting bronchodilator (salbutamol) medication
taken in the past 24 hours for any reason during the evening. The log of the number of weekly puffs of rescue
bronchodilator use was analyzed by the longitudinal mixed effects model. Placebo-adjusted data was reported. Analysis was done on the evaluable subjects in the FAS.

End point type	Secondary

End point timeframe:

Baseline up to Week 12.

Notes:

[105] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	75	75	159
Units: Ratio				
arithmetic mean (standard error)	0.959 (± 0.0757)	0.9661 (± 0.0786)	0.9264 (± 0.0747)	0.9355 (± 0.0612)

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	77			
Units: Ratio				
arithmetic mean (standard error)	0.8375 (± 0.0674)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline (Baseline Dyspnea Index [BDI]) in dyspnea (Transition Dyspnea Index [TDI]) at Weeks 2, 6, 10 and 12

End point title	Change from baseline (Baseline Dyspnea Index [BDI]) in dyspnea (Transition Dyspnea Index [TDI]) at Weeks 2, 6, 10 and 12

End point description:

BDI: 24-item questionnaire to assess baseline dyspnea in 3 domains, functional impairment; magnitude of task; magnitude
of effort. Each item rated on 5-point scale: 0 (very severe), 4 (no impairment). BDI total score range: 0 to 12, lower
score=more severe dyspnea. TDI: 24-item questionnaire to measure changes in dyspnea severity from baseline in same 3
domains, as in BDI. Each item rated on 7-point scale: -3 (major deterioration) to 3 (major improvement). TDI total score
range: -9 to 9, lower score=more deterioration. BDI/TDI total scores were obtained by adding scores for each of 3 domains. Analysis was done on the FAS. "n" signifies subjects with available data at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Baseline; Weeks 2, 6, 10, and 12.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	176[106]	89[107]	88[108]	86[109]
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=171, 88, 83, 83, 171, 84)	0.9237 (± 0.153)	0.9546 (± 0.2132)	1.0733 (± 0.22)	0.9396 (± 0.2195)
Week 6 (n=165, 84, 78, 80, 158, 79)	1.3651 (± 0.1828)	1.3047 (± 0.2558)	1.6243 (± 0.2653)	1.4025 (± 0.2625)
Week 10 (n=160, 79, 74, 77, 147, 70)	1.4391 (± 0.2019)	1.8145 (± 0.2852)	1.3107 (± 0.2951)	1.1386 (± 0.2905)
Week 12 (n=158, 77, 73, 74, 147, 69)	1.9102 (± 0.2092)	2.269 (± 0.2966)	1.592 (± 0.3061)	1.5267 (± 0.3028)

Notes:

[106] - Subjects who were evaluable for this measure.

[107] - Subjects who were evaluable for this measure.

[108] - Subjects who were evaluable for this measure.

[109] - Subjects who were evaluable for this measure.

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175[110]	88[111]		
Units: units on a scale				
arithmetic mean (standard error)				
Week 2 (n=171, 88, 83, 83, 171, 84)	0.7365 (± 0.153)	1.1024 (± 0.2178)		
Week 6 (n=165, 84, 78, 80, 158, 79)	0.9158 (± 0.1857)	1.7519 (± 0.2628)		
Week 10 (n=160, 79, 74, 77, 147, 70)	0.9987 (± 0.208)	1.8776 (± 0.2985)		
Week 12 (n=158, 77, 73, 74, 147, 69)	1.2234 (± 0.2153)	1.6961 (± 0.3105)		

Notes:

[110] - Subjects who were evaluable for this measure.

[111] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with post-baseline electrocardiogram (ECG) measurements meeting categorical summarization criteria

End point title	Percentage of subjects with post-baseline electrocardiogram (ECG) measurements meeting categorical summarization criteria

End point description:

Triplicate 12-lead ECG measurements (each recording separated by 2 to 4 minutes) were performed and the average was
calculated. The time from ECG Q wave to the end of the T wave corresponding to electrical systole (QT) was corrected for
heart rate (QTc). QTc using Fridericia's formula (QTcF) was calculated. Subjects with maximum increase from baseline of
30 to less than (<) 60 milliseconds (msec) and more than or equal to (>=) 60 msec for QTcF were summarized, as were
those with post-baseline absolute (abs) QT values of >=500 msec. Analysis was done on the subjects in the safety analysis set (all randomized subjects who had received at least 1 dose of study drug, regardless of whether they had efficacy data) who had post-baseline ECG data. "n" signifies subjects

with available data for each measurement at each time point for each arm respectively.

End point type	Secondary

End point timeframe:

Weeks 2, 6, 10 and 12; follow-up (Week 14).

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	180[112]	90[113]	89[114]	88[115]
Units: Percentage of subjects				
number (not applicable)				
QTcF: 30- <60 msec, Week 2 (n=175,89,86,85,176,86)	1.1	2.2	1.2	1.2
QTcF: 30- <60 msec, Week 6 (n=169,85,81,81,162,80)	1.8	0	0	3.7
QTcF: 30- <60 msec, Week 10(n=164,79,77,79,152,70)	1.2	1.3	0	5.1
QTcF: 30 - <60 msec, Week12(n=162,79,76,76,150,70)	1.2	1.3	2.6	3.9
QTcF: 30 - <60 msec, Week14(n=162,79,76,75,152,70)	0.6	1.3	2.6	2.7
QTcF: >=60 msec, Week 2(n=175,89,86,85,176,86)	0	0	0	0
QTcF: >=60 msec, Week 6(n=169,85,81,81,162,80)	0	0	0	0
QTcF: >=60 msec, Week 10(n=164,79,77,79,152,70)	0	0	0	0
QTcF: >=60 msec, Week 12(n=162,79,76,76,150,70)	0	0	0	0
QTcF: >=60 msec, Week 14(n=162,79,76,75,152,70)	0	0	0	0
Abs QT >=500 msec, Week 2(n=175,89,86,85,178,86)	0	0	0	0
Abs QT >=500 msec, Week 6(n=169,85,81,82,165,80)	0	0	0	0
Abs QT >=500 msec, Week 10(n=164,81,77,79,154,71)	0	1.2	0	0
Abs QT >=500 msec, Week 12(n=162,80,76,76,154,70)	0	0	0	0
Abs QT >=500 msec, Week 14(n=162,79,76,75,154,70)	0	0	0	0

Notes:

[112] - Subjects who were evaluable for this measure.

[113] - Subjects who were evaluable for this measure.

[114] - Subjects who were evaluable for this measure.

[115] - Subjects who were evaluable for this measure.

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180[116]	89[117]		
Units: Percentage of subjects				
number (not applicable)				
QTcF: 30- <60 msec, Week 2 (n=175,89,86,85,176,86)	6.3	2.3		

QTcF: 30- <60 msec, Week 6 (n=169,85,81,81,162,80)	1.9	0		
QTcF: 30- <60 msec, Week 10(n=164,79,77,79,152,70)	7.2	2.9		
QTcF: 30 - <60 msec, Week12(n=162,79,76,76,150,70)	3.3	5.7		
QTcF: 30 - <60 msec, Week14(n=162,79,76,75,152,70)	0.7	1.4		
QTcF: >=60 msec, Week 2(n=175,89,86,85,176,86)	0	0		
QTcF: >=60 msec, Week 6(n=169,85,81,81,162,80)	0	0		
QTcF: >=60 msec, Week 10(n=164,79,77,79,152,70)	0	0		
QTcF: >=60 msec, Week 12(n=162,79,76,76,150,70)	0	0		
QTcF: >=60 msec, Week 14(n=162,79,76,75,152,70)	0	0		
Abs QT >=500 msec, Week 2(n=175,89,86,85,178,86)	0	0		
Abs QT >=500 msec, Week 6(n=169,85,81,82,165,80)	0	0		
Abs QT >=500 msec, Week 10(n=164,81,77,79,154,71)	0	0		
Abs QT >=500 msec, Week 12(n=162,80,76,76,154,70)	0	0		
Abs QT >=500 msec, Week 14(n=162,79,76,75,154,70)	0	0		

Notes:

[116] - Subjects who were evaluable for this measure.

[117] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with changes from baseline in vital signs values which met criteria for categorical summarization

End point title	Number of subjects with changes from baseline in vital signs values which met criteria for categorical summarization

End point description:

Subjects with supine systolic blood pressure (BP) <90 millimeters of mercury (mmHg), maximum increase and decrease
from baseline supine systolic BP of >=30 mmHg, supine diastolic BP <50 mmHg, and maximum increase and decrease from
baseline supine diastolic BP >=20 mmHg at any time post dose were summarized. Subjects with supine pulse rate (PR)
<40 or >120 beats per minute (bpm) were also summarized. Analysis was done on the subjects in the safety analysis set (all subjects randomized who had received at least 1 dose of study drug, regardless of whether they had efficacy data) who had available vital signs data.

End point type	Secondary

End point timeframe:

Baseline; Week 2 up to Week 14.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	179	90	89	88
Units: Subjects				
Systolic BP <90 mmHg	1	0	0	0
Decrease from baseline systolic BP >=30 mmHg	8	4	4	5
Increase from baseline systolic BP >=30 mmHg	4	2	2	1
Diastolic BP <50 mmHg	0	0	0	0
Decrease from baseline diastolic BP >=20 mmHg	10	5	4	3
Increase from baseline diastolic BP >=20 mmHg	6	3	2	5
Supine PR <40 bpm	0	0	0	0
Supine PR >120 bpm	0	0	0	2

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	89		
Units: Subjects				
Systolic BP <90 mmHg	0	0		
Decrease from baseline systolic BP >=30 mmHg	9	8		
Increase from baseline systolic BP >=30 mmHg	9	1		
Diastolic BP <50 mmHg	0	1		
Decrease from baseline diastolic BP >=20 mmHg	12	5		
Increase from baseline diastolic BP >=20 mmHg	8	5		
Supine PR <40 bpm	0	0		
Supine PR >120 bpm	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with laboratory test abnormalities

End point title	Number of subjects with laboratory test abnormalities

End point description:

Number of subjects with laboratory test abnormalities without regard to baseline abnormality. Laboratory test parameters
included hematology, liver function, renal function, electrolytes, clinical chemistry, and urinalysis (dipstick and microscopy). Analysis was done on subjects in the safety analysis set (all subjects randomized who had received at least 1 dose of study drug, regardless of whether they had efficacy data) who had post-baseline laboratory data.

End point type	Secondary

End point timeframe:

Baseline; Week 2 up to Week 14.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	180	90	89	88
Units: Subjects	150	79	66	76

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	88		
Units: Subjects	144	68		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent adverse events (AEs)

End point title	Number of subjects with treatment-emergent adverse events (AEs)

End point description:

Number of subjects with all causality treatment-emergent adverse events. Analysis was done on the safety analysis set which included all subjects randomized who had received at least 1 dose of study drug, regardless of whether they had efficacy data.

End point type	Secondary

End point timeframe:

Baseline up to Week 14.

End point values	Placebo	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	181	90	91	88
Units: Subjects	72	41	43	45

End point values	PH-797804 6 mg	PH-797804 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	89		
Units: Subjects	103	46		

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FVC at Weeks 0 and 12

End point title	Placebo-adjusted change from baseline in post-study drug, pre-bronchodilator FVC at Weeks 0 and 12[118]

End point description:

FVC is the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. Trough FVC
was obtained from spirometry, performed before study treatment administration. The change from baseline in post-study
drug, pre-bronchodilator FVC at Weeks 0 and 12 was analyzed using the ANCOVA model with treatment as a fixed effect
and baseline value as a covariate. Post-study drug spirometry was performed 15-30 minutes after administration of study
drug at the Weeks 0 and 12 visits. Placebo-adjusted data was reported. Analysis was done on the FAS.
"n" signifies subjects with available data at the specified time point for each arm respectively.

End point type	Secondary

End point timeframe:

Week 0 (randomization) and Week 12.

Notes:

[118] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Placebo-adjusted estimates are reported. As such, there is no data for the placebo arm.

End point values	PH-797804 0.25 mg	PH-797804 1 mg	PH-797804 3 mg	PH-797804 6 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[119]	88[120]	86[121]	175[122]
Units: litre(s)				
arithmetic mean (standard error)				
Week 0 (n=89, 85, 85, 175, 87)	0.0467 (± 0.0259)	0.0159 (± 0.0264)	-0.0127 (± 0.0264)	0.0221 (± 0.0213)
Week 12 (n=77, 72, 72, 146, 69)	-0.0051 (± 0.0237)	-0.0014 (± 0.0243)	-0.0289 (± 0.0243)	-0.0059 (± 0.0196)

Notes:

[119] - Subjects who were evaluable for this measure.

[120] - Subjects who were evaluable for this measure.

[121] - Subjects who were evaluable for this measure.

[122] - Subjects who were evaluable for this measure.

End point values	PH-797804 10 mg			
Subject group type	Reporting group			
Number of subjects analysed	88[123]			
Units: litre(s)				
arithmetic mean (standard error)				

Week 0 (n=89, 85, 85, 175, 87) Week 12 (n=77, 72, 72, 146, 69)	0.0032 (± 0.0262) -0.0159 (± 0.0247)			

Notes:

[123] - Subjects who were evaluable for this measure.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 28 days after last study drug administration.

Adverse event reporting additional description:

All treated subjects were analyzed for adverse events (AEs). The same event may appear as both an AE and an SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo matched to PH-797804 tablet plus tiotropium bromide 18 microgram (mcg) orally once daily for 12 weeks.

Reporting group title	PH-797804 0.25 mg

Reporting group description:

Subjects received PH-797804 0.25 milligram (mg) plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Reporting group title	PH-797804 1 mg

Reporting group description:

Subjects received PH-797804 1 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Reporting group title	PH-797804 3 mg

Reporting group description:

Subjects received PH-797804 3 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Reporting group title	PH-797804 6 mg

Reporting group description:

Subjects received PH-797804 6 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Reporting group title	PH-797804 10 mg

Reporting group description:

Subjects received PH-797804 10 mg plus tiotropium bromide 18 mcg orally once daily for 12 weeks.

Serious adverse events	Placebo	PH-797804 0.25 mg	PH-797804 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 181 (3.31%)	3 / 90 (3.33%)	2 / 91 (2.20%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events		0	0
Injury, poisoning and procedural complications			
Ilium fracture			

subjects affected / exposed	0 / 181 (0.00%)	1 / 90 (1.11%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 90 (1.11%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Convulsion			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 181 (0.00%)	1 / 90 (1.11%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 181 (0.55%)	0 / 90 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			

subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PH-797804 3 mg	PH-797804 6 mg	PH-797804 10 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 88 (3.41%)	6 / 182 (3.30%)	3 / 89 (3.37%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0		0
Injury, poisoning and procedural complications			
Ilium fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 182 (0.55%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 88 (2.27%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 88 (0.00%)	1 / 182 (0.55%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tachycardia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 182 (0.55%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 88 (0.00%)	1 / 182 (0.55%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 88 (1.14%)	3 / 182 (1.65%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 182 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	PH-797804 0.25 mg	PH-797804 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 181 (15.47%)	20 / 90 (22.22%)	16 / 91 (17.58%)
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 181 (0.00%)	0 / 90 (0.00%)	0 / 91 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	14 / 181 (7.73%)	13 / 90 (14.44%)	6 / 91 (6.59%)
occurrences (all)	15	13	6
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 181 (3.31%)	1 / 90 (1.11%)	2 / 91 (2.20%)
occurrences (all)	6	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 181 (6.08%)	7 / 90 (7.78%)	10 / 91 (10.99%)
occurrences (all)	12	7	11

Non-serious adverse events	PH-797804 3 mg	PH-797804 6 mg	PH-797804 10 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 88 (18.18%)	55 / 182 (30.22%)	17 / 89 (19.10%)
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	3 / 88 (3.41%)	10 / 182 (5.49%)	1 / 89 (1.12%)
occurrences (all)	3	10	1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 88 (4.55%)	26 / 182 (14.29%)	10 / 89 (11.24%)
occurrences (all)	5	31	10
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 88 (5.68%)	8 / 182 (4.40%)	5 / 89 (5.62%)
occurrences (all)	5	8	7
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 88 (11.36%)	24 / 182 (13.19%)	4 / 89 (4.49%)
occurrences (all)	10	30	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	Safety-related amendments made: - correction of protocol inconsistency in referring to GOLD updates (should refer to GOLD update 2010 instead of 2009). - updated inclusion criterion regarding female of non-childbearing potential. - updated an exclusion criterion to clarify that sites were allowed to repeat screening lab tests once if they suspected abnormal results were anomalous. - updated an exclusion criterion to clarify that abstinence from intercourse was to be during the study period and not just the ovulation period. - updates to Prohibited Medications section: sponsor would review concomitant medications on a weekly basis as part of data safety review. Also, it was clarified that subjects had to be on tiotropium bromide as background theray for 1 month prior to screening in order to be eligible and were not to be consented to be started on tiotropium bromide solely for the purpose of participating in the study. - Procedures were restructured where applicable to specify that procedures were to be completed from the least to the most invasive. Eg, electrocardiogram (ECG) was to be performed before vitals and blood draw for labs. - updates to Randomization Visit procedures to reflect that salbutamol was not to be taken daily and also clarifications where applicable on how salbutamol was to be administered. - addition of text to clarify that full physical examination included vital sign and blood pressure measurements. - updates to ensure sites knew that weekly phone calls to subjects were to start after Screening Visit. - updates to clarify that any subject with clinically significant finding on ECG was to have appropriate follow-up. - addition of text to clarify details of COPD symptoms, exacerbations, and rescue bronchodilator usage analyses. - clarified that unblinded safety review by Internal Review Committee was to be conducted after approximately 1/3 and 2/3 of subjects have been randomized. - tuberculosis testing algorithm diagram updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Subject disposition and baseline characteristics are provided for treated subjects only.

Notes: