



Clinical trial results:

A Randomized, Double-Blind, Two Treatment, Two Period, Chronic Dosing (2 Weeks), Cross-Over, Single-Center Study to Evaluate the Effects of PT003 and Placebo MDI on Specific Image Based Airway Volumes and Resistance in Subjects With Moderate to Severe COPD

Summary

EudraCT number	2015-001743-36
Trial protocol	BE
Global end of trial date	26 January 2017

Results information

Result version number	v1 (current)
This version publication date	03 March 2018
First version publication date	03 March 2018

Trial information

Trial identification

Sponsor protocol code	PT003018
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02643082
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pearl Therapeutics, Inc.
Sponsor organisation address	280 Headquarters Plaza, Morristown, United States, 07960
Public contact	Pearl Therapeutics, Inc., Pearl Therapeutics, Inc., 1 6503052600, creisner@pearltherapeutics.com
Scientific contact	Pearl Therapeutics, Inc., Pearl Therapeutics, Inc., 1 6503052600, creisner@pearltherapeutics.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	26 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 January 2017
Global end of trial reached?	Yes
Global end of trial date	26 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of treatment with GFF MDI, twice daily (BID) compared with Placebo MDI on specific image-based airway volumes and resistance in subjects with moderate to severe chronic obstructive pulmonary disease (COPD) following chronic dosing after approximately two weeks treatment.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	6
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 1 site in Antwerp Belgium from January 2016 to December 2016. The study was anticipated to run for approximately 9 months but not to exceed 12 months. The study period was duration was expected to run approximately 13 weeks for each subject.

Pre-assignment

Screening details:

Subjects were randomized into 1 of 2 treatment sequences: subjects in Sequence 1 received GFF MDI in Treatment Period 1 followed by Placebo MDI in Treatment Period 2, and subjects in Sequence 2 received Placebo MDI in Treatment Period 1 followed by GFF MDI in Treatment Period 2. By sequence treatment tabulations were not pre-specified

Period 1

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

Blinding implementation details:

Study staff were blinded with exception of the Study Pharmacist.

Arms

Arm title	Overall Study
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Arm description:

All Randomized Patients

Arm type	Experimental
Investigational medicinal product name	Glycopyrronium Formoterol Fumarate MDI
Investigational medicinal product code	
Other name	GFF MDI
Pharmaceutical forms	Pressurised inhalation, suspension
Routes of administration	Inhalation use

Dosage and administration details:

GFF MDI 14.4/9.6 ug 2 inhalations twice a day

Investigational medicinal product name	Placebo MDI
Investigational medicinal product code	
Other name	Placebo MDI
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

2 inhalations twice a day

Number of subjects in period 1	Overall Study
Started	20
Treated with GFF MDI 14.4/9.6 µg	20
Treated with Placebo MDI	19
Completed	19
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
Reporting group description:	
All Randomized Patients	

Reporting group values	Overall Study	Total	
Number of subjects	20	20	
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	14	14	
Age Continuous			
Units: years			
arithmetic mean	64.8	-	
standard deviation	± 8.9		
Sex: Female, Male			
Units: Subjects			
Female	5	5	
Male	15	15	
Race			
Units: Subjects			
White	20	20	

Subject analysis sets

Subject analysis set title	GFF MDI 14.4/9.6 µg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
GFF MDI	
Subject analysis set title	Placebo MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Placebo	

Reporting group values	GFF MDI 14.4/9.6 µg	Placebo MDI	
Number of subjects	20	19	
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	14	13	
Age Continuous			
Units: years			
arithmetic mean	64.8	64.7	
standard deviation	± 8.7	± 9.0	

Sex: Female, Male			
Units: Subjects			
Female			
Male			
Race			
Units: Subjects			
White	20	19	

End points

End points reporting groups

Reporting group title	Overall Study
Reporting group description: All Randomized Patients	
Subject analysis set title	GFF MDI 14.4/9.6 µg
Subject analysis set type	Intention-to-treat
Subject analysis set description: GFF MDI	
Subject analysis set title	Placebo MDI
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo	

Primary: Specific Airway Volume (siVaw)

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

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Each arm should document the number of subjects who started and the number who completed. However, there is a system limitation at the moment with this option for the reporting of the statistical analysis. There is an automated sum up of the arms population that is performed by the system which is not valid for this option. The result can be reported by omitting the statistical Analysis.

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: mL/L				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	1.79 (1.48 to 2.16)	1.02 (0.85 to 1.24)	

Statistical analyses

No statistical analyses for this end point

Primary: Specific Airway Resistance (siRaw)

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

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Each arm should document the number of subjects who started and the number who completed. However, there is a system limitation at the moment with this option for the reporting of the statistical analysis. There is an automated sum up of the arms population that is performed by the system which is not valid for this option. The result can be reported by omitting the statistical Analysis.

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: kPa s				
geometric mean (confidence interval 95%)	99999999 (99999999 to 999999999)	0.09 (0.07 to 0.11)	0.30 (0.23 to 0.40)	

Statistical analyses

No statistical analyses for this end point

Secondary: Airway Resistance (iRaw)

End point title	Airway Resistance (iRaw)
End point description:	iRaw represents the airway resistance, averaged across lobes, without correction for lung lobe volume
End point type	Secondary
End point timeframe:	
Day 15	

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: kPa s/L				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.07 (0.06 to 0.10)	0.25 (0.19 to 0.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Airway Volume (iVaw)

End point title	Airway Volume (iVaw)
End point description:	iVaw represents the airway Volume, averaged across lobes, without correction for lung lobe volume
End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: mL				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	2.11 (1.73 to 2.58)	1.18 (0.97 to 1.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FEV1 (L) at Day 15

End point title	Change From Baseline in FEV1 (L) at Day 15
End point description:	Change from baseline in Forced Expiratory Volume at 1 second
End point type	Secondary
End point timeframe:	Day 15

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: Liters				
least squares mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.334 (0.245 to 0.422)	-0.110 (-0.198 to -0.022)	

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to Baseline in FRC (L) at Day 15

End point title	Ratio to Baseline in FRC (L) at Day 15
End point description:	Change from baseline in Functional Residual Capacity
End point type	Secondary

End point timeframe:

Day 15

End point values	Overall Study	GFF MDI 14.4/9.6 µg	Placebo MDI	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	20	19	
Units: Liters				
geometric mean (confidence interval 95%)	999999999 (999999999 to 999999999)	0.90 (0.86 to 0.93)	1.03 (0.99 to 1.07)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time the subject signed consent up to the follow-up phone call 7-14 days after last dose of study drug.

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Overall Study
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Reporting group description:

All Randomized Patients

Reporting group title	Placebo MDI
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Reporting group description:

Placebo

Reporting group title	GFF MDI 14.4/9.6 µg
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Reporting group description:

GFF MDI

Serious adverse events	Overall Study	Placebo MDI	GFF MDI 14.4/9.6 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Non-serious adverse events	Overall Study	Placebo MDI	GFF MDI 14.4/9.6 µg
Total subjects affected by non-serious adverse events subjects affected / exposed	15 / 20 (75.00%)	8 / 19 (42.11%)	12 / 20 (60.00%)
Vascular disorders			
Hypertension subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Cardiac disorders			
Acute Coronary Syndrome subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Acute Myocardial Infarction subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Bradycardia subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Dizziness subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Headache subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	3	1	2
Tremor subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	3	1	2
Dysgeusia subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Oedema subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1
Toothache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	3 / 19 (15.79%) 3	0 / 20 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 19 (0.00%) 0	2 / 20 (10.00%) 2
Obstructive Airway Disorder subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Pulmonary Mass subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	0 / 19 (0.00%) 0	1 / 20 (5.00%) 2
Rales subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1
Renal and urinary disorders			
Renal Mass subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Renal Pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal Pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0
Infections and infestations			
Respiratory Tract Infection			

subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 19 (0.00%) 0	2 / 20 (10.00%) 2
Pneumonia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1
Metabolism and nutrition disorders Iron Deficiency subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

We have provided the mean and 95% CI for each treatment and endpoint. This value is NA and has been entered as 999999999. For all endpoints except FEV1 we input values as Geometric LS Mean however this choice was NA and Geometric Mean was selected.
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Notes: