Clinical trial results:
An Open Label Placebo Study To Assess The Inhalation Profile Obtained By Acoustic Monitoring In COPD Patients Using The NEXThaler® Dry Powder Inhaler (DPI) Device.

Summary

EudraCT number	2013-000262-11
Trial protocol	IT
Global end of trial date	26 June 2014

Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	09 August 2015

Trial information

Trial identification

Sponsor protocol code	CCD_01535BC1_01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02018549
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Chiesi Farmaceutici S.p.A.
Sponsor organisation address	Via Palermo 26/A, Parma, Italy, 43122
Public contact	Project Management unit, CROMSOURCE, 0039 0458222811, jenny.zecchini@cromsource.com
Scientific contact	Project Management unit, CROMSOURCE, 0039 0458222811, jenny.zecchini@cromsource.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 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2014
Global end of trial reached?	Yes
Global end of trial date	26 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the inspiration profile through the NEXThaler® device in COPD patients with varying degrees of airflow limitation as per GOLD 2013 (updated) spirometric classification of disease severity.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines and local law requirements . Other than routine care, no specific measures for protection of trial subjects were implemented.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2013
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	Italy: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	23
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Seventy-two patients in total were screened and enrolled in the study. Twenty-one patients were in COPD GOLD stage I, 20 in stage II, 21 in stage III and 10 in stage IV. All enrolled patients completed the study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	NEXThaler® dry powder inhaler with placebo

Arm description:

NEXThaler® dry powder inhaler containing placebo, two inhalations in the morning during the only study visit

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

Dosage and administration details:

NEXThaler® dry powder inhaler containing placebo two inhalations in the morning during the study visit

Number of subjects in period 1	NEXThaler® dry powder inhaler with placebo
Started	72
Completed	72

Baseline characteristics

Reporting groups	
Reporting group title	NEXThaler® dry powder inhaler with placebo
Reporting group description:	
NEXThaler® dry powder inhaler containing placebo, two inhalations in the morning during the only study visit	

Reporting group values	NEXThaler® dry powder inhaler with placebo	Total	
Number of subjects	72	72	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Adults (18-64 years)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
From 65-84 years	49	49	
85 years and over	0	0	
Adults 18-64 y	23	23	
Age continuous			
Data are based on per protocol population			
Units: years			
arithmetic mean	64.9		
standard deviation	± 8.4	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	60	60	

Subject analysis sets	
Subject analysis set title	Test treatment, GOLD I - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD II - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD III - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD IV - Enrolled/Safety

Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD I - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD II - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD III - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD IV - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	

Reporting group values	Test treatment, GOLD I - Enrolled/Safety	Test treatment, GOLD II - Enrolled/Safety	Test treatment, GOLD III - Enrolled/Safety
Number of subjects	21	20	21
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Adults (18-64 years)			
Children (2-11 years)			
Adolescents (12-17 years)			
From 65-84 years			
85 years and over			
Adults 18-64 y			
Age continuous			
Data are based on per protocol population			
Units: years			
arithmetic mean	64.9	68.2	70.4
standard deviation	± 8.4	± 7.3	± 8.2
Gender categorical			
Units: Subjects			
Female	8	2	2
Male	13	18	19

Reporting group values	Test treatment, GOLD IV - Enrolled/Safety	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol

Number of subjects	10	19	20
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Adults (18-64 years)			
Children (2-11 years)			
Adolescents (12-17 years)			
From 65-84 years			
85 years and over			
Adults 18-64 y			
Age continuous			
Data are based on per protocol population			
Units: years			
arithmetic mean	67.8	64.9	68.2
standard deviation	± 9.5	± 8.4	± 7.3
Gender categorical			
Units: Subjects			
Female	0	7	2
Male	10	12	18

Reporting group values	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol	
Number of subjects	20	10	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Adults (18-64 years)			
Children (2-11 years)			
Adolescents (12-17 years)			
From 65-84 years			
85 years and over			
Adults 18-64 y			
Age continuous			
Data are based on per protocol population			
Units: years			
arithmetic mean	70.4	67.8	
standard deviation	± 8.2	± 9.5	
Gender categorical			
Units: Subjects			
Female	2	0	
Male	18	10	

End points

End points reporting groups

Reporting group title	NEXThaler® dry powder inhaler with placebo
Reporting group description: NEXThaler® dry powder inhaler containing placebo, two inhalations in the morning during the only study visit	
Subject analysis set title	Test treatment, GOLD I - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD II - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD III - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD IV - Enrolled/Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received the study medication	
Subject analysis set title	Test treatment, GOLD I - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD II - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD III - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	
Subject analysis set title	Test treatment, GOLD IV - Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All patients from the Safety population excluding patients without any valid evaluation of inhalation profile or with major protocol deviations significantly affecting this assessment	

Primary: Flow at BAM - first inhalation

End point title	Flow at BAM - first inhalation[1]
End point description: Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.	
End point type	Primary
End point timeframe: At each of the two inhalations during the only visit	

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: No statistical analysis was completed for this enpoint

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: L/min				
arithmetic mean (standard deviation)	42.9 (± 6.38)	40.27 (± 4.2)	41.05 (± 7.04)	44.76 (± 7.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to BAM firing

End point title	Time to BAM firing

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: sec				
arithmetic mean (standard deviation)	0.17 (± 0.14)	0.17 (± 0.12)	0.18 (± 0.12)	0.2 (± 0.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Initial acceleration

End point title	Initial acceleration

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: L/min/sec				
arithmetic mean (standard deviation)	155.6 (± 65.5)	140.3 (± 55.1)	140.4 (± 37.4)	158.7 (± 42.4)

Statistical analyses

No statistical analyses for this end point

Secondary: PIF

End point title	PIF

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: L/min				
arithmetic mean (standard deviation)	74.08 (± 20.79)	69.13 (± 17.67)	63.47 (± 14.96)	63.51 (± 20.15)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PIF

End point title	Time to PIF

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: sec				
arithmetic mean (standard deviation)	0.72 (± 0.34)	0.64 (± 0.26)	0.63 (± 0.3)	0.57 (± 0.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Total inhaled volume

End point title	Total inhaled volume

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: liters				
arithmetic mean (standard deviation)	2.28 (± 0.6)	1.7 (± 0.6)	1.75 (± 0.73)	1.51 (± 0.62)

Statistical analyses

No statistical analyses for this end point

Secondary: Total inhalation time

End point title	Total inhalation time

End point description:

Variables were measured by acoustic monitoring technology through the NEXThaler® during the inspiratory manoeuvre. Only data on the first inhalation are reported here.

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: sec				
arithmetic mean (standard deviation)	2.9 (± 0.68)	2.29 (± 0.6)	2.39 (± 0.79)	2.12 (± 0.8)

Statistical analyses

No statistical analyses for this end point

Secondary: FEV1

End point title	FEV1
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: liters				
arithmetic mean (standard deviation)	2.03 (± 0.45)	1.57 (± 0.47)	1.08 (± 0.22)	0.74 (± 0.2)

Statistical analyses

No statistical analyses for this end point

Secondary: FEV1 % predicted

End point title	FEV1 % predicted
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: percent				
arithmetic mean (standard deviation)	73.4 (± 10.3)	50.5 (± 10.9)	36.5 (± 8.6)	22.4 (± 4.1)

Statistical analyses

No statistical analyses for this end point

Secondary: FVC

End point title	FVC
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: liters				
arithmetic mean (standard deviation)	3.36 (± 0.72)	2.77 (± 0.59)	2.31 (± 0.43)	2.11 (± 0.5)

Statistical analyses

No statistical analyses for this end point

Secondary: FVC % predicted

End point title	FVC % predicted
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: percent				
arithmetic mean (standard deviation)	95.5 (± 10.7)	69.6 (± 8.6)	60 (± 13)	50 (± 12.8)

Statistical analyses

No statistical analyses for this end point

Secondary: FEV1/FVC

End point title	FEV1/FVC
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: integer				
arithmetic mean (standard deviation)	0.61 (± 0.04)	0.56 (± 0.08)	0.47 (± 0.09)	0.36 (± 0.09)

Statistical analyses

No statistical analyses for this end point

Secondary: PEF

End point title	PEF
End point description:	
Pulmonary function data are based on spirometry	
End point type	Secondary
End point timeframe:	
At each of the two inhalations during the only visit	

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: L/min				
arithmetic mean (standard deviation)	365.1 (± 106.7)	292 (± 103.2)	197.3 (± 60.8)	160.9 (± 38.5)

Statistical analyses

No statistical analyses for this end point

Secondary: PEF % predicted

End point title	PEF % predicted

End point description:

Pulmonary function data are based on spirometry

End point type	Secondary

End point timeframe:

At each of the two inhalations during the only visit

End point values	Test treatment, GOLD I - Per protocol	Test treatment, GOLD II - Per protocol	Test treatment, GOLD III - Per protocol	Test treatment, GOLD IV - Per protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	20	10
Units: percent				
arithmetic mean (standard deviation)	87.1 (± 15.9)	64.4 (± 20.2)	45 (± 12.5)	33.7 (± 7.3)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

not specified

Adverse event reporting additional description:

Any adverse events or serious adverse events occurring since the signature of the informed consent were recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Safety population - Test treatment

Reporting group description:

All patients who received the study medication.

Serious adverse events	Safety population - Test treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety population - Test treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: There were no treatment-emergent adverse events (TEAEs) in any patient (p.45 CSR).

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.

No limitations or caveats are applicable to this trial

Notes: