Clinical trial results:
A 12-week, multicenter, randomized, double-blind, double-dummy, 2-arm parallel group study comparing the efficacy and safety of Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg/actuation), 2 inhalations b.i.d., versus Seretide® Accuhaler® (fluticasone 250 µg plus salmeterol 50 µg/actuation), 1 inhalation b.i.d., on small airway derived parameters in patients with asthma.

Summary

EudraCT number	2011-003449-17
Trial protocol	IT
Global end of trial date	24 February 2014

Results information

Result version number	v1 (current)
This version publication date	11 July 2016
First version publication date	09 August 2015

Trial information

Trial identification

Sponsor protocol code	MC-PR-15009-001-11

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01570478
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	Clinical Trial Transparency Manager, Chiesi Farmaceutici S.p.A., ClinicalTrials_info@chiesi.com
Scientific contact	Clinical Trial Transparency Manager, Chiesi Farmaceutici S.p.A., ClinicalTrials_info@chiesi.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	24 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2014
Global end of trial reached?	Yes
Global end of trial date	24 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the higher efficacy of Foster® NEXThaler® 100/6 extra fine (two inhalations b.i.d.) versus Seretide® Accuhaler® 250/50 (one inhalation b.i.d.), in terms of pulmonary function (change from baseline to the end of treatment in post-dose peripheral airway resistance) in patients with asthma.

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:

After a pre-screening visit (Visit 0 at week -5 before the randomization visit) and a screening visit (Visit 1 at week -4), the study plan foresees a 4-week run-in period where patients will receive a standardised treatment with Seretide® Accuhaler® 250/50 µg, 1 inhalation b.i.d. (daily dose of FP 500 µg plus SALM 100 µg) and have any non-permitted medications withdrawn prior to entry into test treatment period.

Evidence for comparator: -

Actual start date of recruitment	06 July 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	Italy: 108
Worldwide total number of subjects	108
EEA total number of subjects	108

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)	108
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 149 patients were screened and 41 of them were not randomised, mainly for ineligibility. Therefore, 108 patients in total were randomised to receive the assigned treatment: 54 were assigned to the Foster® NEXThaler® group (Foster®) and 54 were assigned to the Seretide® Accuhaler® group (Seretide®).

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The realization of the double-blind design was made possible by the use of a Foster® NEXThaler® and Seretide® Accuhaler® placebo, which was totally indistinguishable from the respective active in terms of size, shape, colour and mode of inhalation. Each placebo was administered together with the alternate active ingredient (p.28 CSR).

Arms

Are arms mutually exclusive?	Yes
Arm title	Test treatment

Arm description:

Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg per actuation), 2 inhalations b.i.d. (daily dose of BDP 400 µg plus FF 24 µg) plus Seretide® Accuhaler® placebo, 1 inhalation b.i.d.

Arm type	Experimental
Investigational medicinal product name	Foster® NEXThaler®
Investigational medicinal product code	
Other name	BDP /FF NEXThaler, beclomethasone dipropionate, formoterol fumarate
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg per actuation), 2 inhalations b.i.d.
(daily dose of BDP 400 µg plus FF 24 µg) plus Seretide® Accuhaler® placebo, 1 inhalation b.i.d.

Arm title	Reference treatment

Arm description:

Seretide Accuhaler: fixed combination of fluticasone propionate 250 µg plus salmeterol xinafoate 50 µg per actuation. (daily dose of FP 500 µg plus SX 100 µg) plus Foster® NEXThaler® placebo, 2 inhalations b.i.d.

Arm type	Active comparator
Investigational medicinal product name	Seretide® Accuhaler
Investigational medicinal product code	
Other name	fluticasone propionate, salmeterol xinafoate
Pharmaceutical forms	Inhalation powder, pre-dispensed
Routes of administration	Inhalation use

Dosage and administration details:

Seretide® Accuhaler® (fluticasone propionate 250 µg plus salmeterol xinafoate 50 µg per actuation), 1

inhalation b.i.d. (daily dose of fluticasone 500 µg plus salmeterol 100 µg) plus Foster® NEXThaler® placebo, 2 inhalations b.i.d.

Number of subjects in period 1	Test treatment	Reference treatment
Started	54	54
Completed	49	46
Not completed	5	8
Consent withdrawn by subject	3	6
Inclusion/exclusion criteria not met	-	2
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Test treatment
Reporting group description:	
Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg per actuation), 2 inhalations b.i.d. (daily dose of BDP 400 µg plus FF 24 µg) plus Seretide® Accuhaler® placebo, 1 inhalation b.i.d.	
Reporting group title	Reference treatment
Reporting group description:	
Seretide Accuhaler: fixed combination of fluticasone propionate 250 µg plus salmeterol xinafoate 50 µg per actuation. (daily dose of FP 500 µg plus SX 100 µg) plus Foster® NEXThaler® placebo, 2 inhalations b.i.d.	

Reporting group values	Test treatment	Reference treatment	Total
Number of subjects	54	54	108
Age categorical Units: Subjects			
Adults (18-64 years)	54	54	108
Age continuous Units: years			
arithmetic mean	50.2	51	
standard deviation	± 15.7	± 16.1	-
Gender categorical Units: Subjects			
Female	13	19	32
Male	41	35	76

Subject analysis sets	
Subject analysis set title	ITT Population - Test treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients who receive at least one administration of the study medication and with at least one available postbaseline efficacy evaluation	
Subject analysis set title	ITT Population - Reference treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients who receive at least one administration of the study medication and with at least one available postbaseline efficacy evaluation	
Subject analysis set title	Safety population - Test treatment
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least one administration of the study medication.	
Subject analysis set title	safety population - Reference treatment
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least one administration of the study medication.	

Reporting group values	ITT Population - Test treatment	ITT Population - Reference treatment	Safety population - Test treatment
Number of subjects	54	54	54
Age categorical			
Units: Subjects			
Adults (18-64 years)			
Age continuous			
Units: years			
arithmetic mean	50.2	51	50.2
standard deviation	± 15.7	± 16.1	± 15.7
Gender categorical			
Units: Subjects			
Female	13	19	13
Male	41	35	41

Reporting group values	safety population - Reference treatment		
Number of subjects	54		
Age categorical			
Units: Subjects			
Adults (18-64 years)			
Age continuous			
Units: years			
arithmetic mean	51		
standard deviation	± 16.1		
Gender categorical			
Units: Subjects			
Female	19		
Male	35		

End points

End points reporting groups

Reporting group title	Test treatment
Reporting group description:	
Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg per actuation), 2 inhalations b.i.d. (daily dose of BDP 400 µg plus FF 24 µg) plus Seretide® Accuhaler® placebo, 1 inhalation b.i.d.	
Reporting group title	Reference treatment
Reporting group description:	
Seretide Accuhaler: fixed combination of fluticasone propionate 250 µg plus salmeterol xinafoate 50 µg per actuation. (daily dose of FP 500 µg plus SX 100 µg) plus Foster® NEXThaler® placebo, 2 inhalations b.i.d.	
Subject analysis set title	ITT Population - Test treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients who receive at least one administration of the study medication and with at least one available postbaseline efficacy evaluation	
Subject analysis set title	ITT Population - Reference treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients who receive at least one administration of the study medication and with at least one available postbaseline efficacy evaluation	
Subject analysis set title	Safety population - Test treatment
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least one administration of the study medication.	
Subject analysis set title	safety population - Reference treatment
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least one administration of the study medication.	

Primary: Change from baseline to end of treatment in post-dose peripheral airway resistance [R(5Hz) - R(20Hz)]

End point title	Change from baseline to end of treatment in post-dose peripheral airway resistance [R(5Hz) - R(20Hz)]
End point description:	
Peripheral airway resistance (R5-R20) was measured by Impulse Oscillometry as the difference between total airway resistance (R5) and central airway resistance (R20)	
End point type	Primary
End point timeframe:	
From Vist 1 to Visit 5 (week 12)	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.06 (± 0.085)	-0.064 (± 0.081)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.928
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.025
upper limit	0.027

Secondary: Changes from baseline at each clinic visit in pre-dose R5 (total airway resistance)

End point title	Changes from baseline at each clinic visit in pre-dose R5 (total airway resistance)
End point description:	
Total airway resistance (R5) was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit, from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.029 (± 0.124)	-0.051 (± 0.143)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	0.016
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.034
upper limit	0.065

Secondary: Changes from baseline at each clinic visit in post-dose R5 (total airway resistance)

End point title	Changes from baseline at each clinic visit in post-dose R5 (total airway resistance)

End point description:

Total airway resistance (R5) was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.1 (± 0.124)	-0.098 (± 0.117)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.049
upper limit	0.037

Secondary: Changes from baseline at each clinic visit in pre-dose R20 (central airway resistance)

End point title	Changes from baseline at each clinic visit in pre-dose R20 (central airway resistance)

End point description:

Central airway resistance (R20) was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.008 (± 0.064)	-0.021 (± 0.071)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.444
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	0.035

Secondary: Changes from baseline at each clinic visit in post-dose R20 (central airway resistance)

End point title	Changes from baseline at each clinic visit in post-dose R20 (central airway resistance)

End point description:

Central airway resistance (R20) was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.04 (± 0.071)	-0.035 (± 0.057)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.007
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.032
upper limit	0.017

Secondary: Changes from baseline at each clinic visit in pre-dose R5 - R20 (peripheral airway resistance)

End point title	Changes from baseline at each clinic visit in pre-dose R5 - R20 (peripheral airway resistance)

End point description:

Peripheral airway resistance (R5-R20) was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.021 (± 0.094)	-0.03 (± 0.098)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.029
upper limit	0.04

Secondary: Changes from baseline at each clinic visit in post-dose R5 - R20 (peripheral airway resistance)

End point title	Changes from baseline at each clinic visit in post-dose R5 - R20 (peripheral airway resistance)

End point description:

Peripheral airway resistance (R5 - R20) was measured by Impulse Oscillometry. Only data from Visit 4 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.072 (± 0.075)	-0.055 (± 0.08)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Reference treatment v ITT Population - Test treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.049
upper limit	0.002

Secondary: Changes from baseline at each clinic visit in pre-dose R5 - R20/R5

End point title	Changes from baseline at each clinic visit in pre-dose R5 - R20/R5

End point description:

R5 and R20 were measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.05 (± 0.21)	-0.081 (± 0.235)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.595
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.059
upper limit	0.103

Secondary: Changes from baseline at each clinic visit in post-dose R5 - R20/R5

End point title	Changes from baseline at each clinic visit in post-dose R5 - R20/R5

End point description:

R5 and R20 were measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	-0.16 (± 0.2)	-0.162 (± 0.193)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.901
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.071
upper limit	0.063

Secondary: Changes from baseline at each clinic visit in pre-dose distal capacitive reactance at 5 Hz (X5)

End point title	Changes from baseline at each clinic visit in pre-dose distal capacitive reactance at 5 Hz (X5)
End point description:	
Distal capacitive reactance at 5 Hz was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	0.01 (± 0.13)	0.029 (± 0.099)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.416
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.016
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.053
upper limit	0.022

Secondary: Changes from baseline at each clinic visit in post-dose distal capacitive reactance at 5 Hz (X5)

End point title	Changes from baseline at each clinic visit in post-dose distal capacitive reactance at 5 Hz (X5)

End point description:

Distal capacitive reactance at 5 Hz was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: kPa/L/s				
arithmetic mean (standard deviation)	0.047 (± 0.118)	0.046 (± 0.08)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.696
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.03

Secondary: Changes from baseline at each clinic visit in pre-dose resonant frequency (Fres)

End point title	Changes from baseline at each clinic visit in pre-dose resonant frequency (Fres)

End point description:

Resonant frequency was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: Hz				
arithmetic mean (standard deviation)	-1.62 (± 3.86)	-3.11 (± 5.19)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.275

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	2.87

Secondary: Changes from baseline at each clinic visit in post-dose resonant frequency (Fres)

End point title	Changes from baseline at each clinic visit in post-dose resonant frequency (Fres)

End point description:

Resonant frequency was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: Hz				
arithmetic mean (standard deviation)	-4.94 (± 4.6)	-4.85 (± 5.55)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.678
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.363
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	1.365

Secondary: Changes from baseline at each clinic visit in pre-dose area of reactance

(AX)	
End point title	Changes from baseline at each clinic visit in pre-dose area of reactance (AX)
End point description:	
The area of reactance was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5.	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: Hz*kPa/L/s				
arithmetic mean (standard deviation)	-0.119 (± 1.103)	-0.448 (± 1.224)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Reference treatment v ITT Population - Test treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.693

Secondary: Changes from baseline at each clinic visit in post-dose area of reactance (AX)	
End point title	Changes from baseline at each clinic visit in post-dose area of reactance (AX)
End point description:	
Area of reactance was measured by Impulse Oscillometry. Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: Hz*kPa/L/s				
arithmetic mean (standard deviation)	-0.694 (± 1.071)	-0.788 (± 1.067)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.891
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.265
upper limit	0.305

Secondary: Changes from baseline at each clinic visit in pre-dose residual volume (RV)

End point title	Changes from baseline at each clinic visit in pre-dose residual volume (RV)

End point description:

Residual volume was measured by plethysmographic assessment. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.04 (± 0.382)	-0.037 (± 0.452)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.693
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.217
upper limit	0.145

Secondary: Changes from baseline at each clinic visit in post-dose residual volume (RV)

End point title	Changes from baseline at each clinic visit in post-dose residual volume (RV)

End point description:

Residual volume was measured by plethysmographic assessment. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.09 (± 0.443)	-0.007 (± 0.537)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.245
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.125
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.338
upper limit	0.088

Secondary: Changes from baseline at each clinic visit in pre-dose inspiratory capacity/total lung capacity (IC/TLC)

End point title	Changes from baseline at each clinic visit in pre-dose inspiratory capacity/total lung capacity (IC/TLC)
End point description:	
Inspiratory capacity/total lung capacity was measured by plethysmographic assessment. Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: percentage				
arithmetic mean (standard deviation)	-0.178 (± 6.562)	-0.417 (± 8.38)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.772
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.372
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.168
upper limit	2.912

Secondary: Changes from baseline at each clinic visit in post-dose inspiratory capacity/total lung capacity (IC/TLC)

End point title	Changes from baseline at each clinic visit in post-dose inspiratory capacity/total lung capacity (IC/TLC)

End point description:

Inspiratory capacity/total lung capacity was measured by plethysmographic assessment. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: percentage				
arithmetic mean (standard deviation)	1.596 (± 7.03)	-1.389 (± 7.846)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.221
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.696
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.046
upper limit	4.438

Secondary: Changes from baseline at each clinic visit in pre-dose functional residual capacity (FRC)

End point title	Changes from baseline at each clinic visit in pre-dose functional residual capacity (FRC)

End point description:

Functional residual capacity was measured by plethysmographic assessment. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.079 (± 0.511)	0.101 (± 0.732)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.205

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.04

Secondary: Changes from baseline at each clinic visit in post-dose functional residual capacity (FRC)

End point title	Changes from baseline at each clinic visit in post-dose functional residual capacity (FRC)

End point description:

Functional residual capacity was measured by plethysmographic assessment. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.129 (± 0.486)	0.165 (± 0.762)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.252
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.505
upper limit	0.001

Secondary: Changes from baseline at each clinic visit in pre-dose FEV1	
End point title	Changes from baseline at each clinic visit in pre-dose FEV1
End point description: Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe: At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.059 (± 0.264)	0.051 (± 0.244)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.095
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.197
upper limit	0.007

Secondary: Changes from baseline at each clinic visit in post-dose FEV1	
End point title	Changes from baseline at each clinic visit in post-dose FEV1
End point description: Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe: At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	0.108 (± 0.242)	0.148 (± 0.279)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.557
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.031
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.134
upper limit	0.073

Secondary: Changes from baseline at each clinic visit in pre-dose forced expiratory vital capacity/slow inspiratory vital capacity (FVC/ISVC)

End point title	Changes from baseline at each clinic visit in pre-dose forced expiratory vital capacity/slow inspiratory vital capacity (FVC/ISVC)
End point description:	
Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: integer				
arithmetic mean (standard deviation)	0.004 (± 0.075)	-0.036 (± 0.112)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Reference treatment v ITT Population - Test treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.051

Secondary: Changes from baseline at each clinic visit in post-dose forced expiratory vital capacity/slow inspiratory vital capacity (FVC/ISVC)

End point title	Changes from baseline at each clinic visit in post-dose forced expiratory vital capacity/slow inspiratory vital capacity (FVC/ISVC)
End point description:	
Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: integer				
arithmetic mean (standard deviation)	0.026 (± 0.128)	-0.025 (± 0.102)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.092
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.006
upper limit	0.078

Secondary: Changes from baseline at each clinic visit in pre-dose FEF25-75%

End point title	Changes from baseline at each clinic visit in pre-dose FEF25-75%
End point description:	
Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.025 (± 0.46)	0.127 (± 0.569)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.137
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.342
upper limit	0.068

Secondary: Changes from baseline at each clinic visit in post-dose FEF25-75%

End point title	Changes from baseline at each clinic visit in post-dose FEF25-75%
End point description:	
Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe:	
At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	0.402 (± 0.567)	0.345 (± 0.752)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.609
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.069
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.198
upper limit	0.335

Secondary: Changes from baseline at each clinic visit in pre-dose FEF50%

End point title	Changes from baseline at each clinic visit in pre-dose FEF50%
End point description: Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe: At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	-0.165 (± 0.598)	0.07 (± 0.647)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.069
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.478
upper limit	0.018

Secondary: Changes from baseline at each clinic visit in post-dose FEF50%

End point title	Changes from baseline at each clinic visit in post-dose FEF50%
End point description: Only data from Visit 5 are reported here.	
End point type	Secondary
End point timeframe: At each clinic visit from Visit 1 to Visit 5	

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: liters				
arithmetic mean (standard deviation)	0.39 (± 0.671)	0.428 (± 0.765)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.296
upper limit	0.308

Secondary: Severe asthma exacerbations

End point title	Severe asthma exacerbations

End point description:

Severe asthma exacerbations between date of Visit 2 and the end of the study are considered for the analysis.

End point type	Secondary

End point timeframe:

At each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: integer	1	1		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Test treatment v ITT Population - Reference treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.949
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.059
upper limit	15.171

Secondary: Change from baseline in average asthma symptom score

End point title	Change from baseline in average asthma symptom score

End point description:

Total asthma symptom score has been calculated as sum of total day-time asthma symptom score and total night-time asthma symptom score of a day.
"Overall" data are reported here.

End point type	Secondary

End point timeframe:

Daily from Visit 1 to Visit 5.

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: integer				
arithmetic mean (standard deviation)	-0.438 (± 2.509)	-0.517 (± 1.567)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in percentage of asthma symptom-free days

End point title	Change from baseline in percentage of asthma symptom-free days

End point description:

An asthma symptom-free day is a day with total asthma symptom score = 0."Overall" data are reported here

End point type	Secondary

End point timeframe:

Daily, at each clinic visit from Visit 1 to Visit 5.

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: days				
arithmetic mean (standard deviation)	5.9 (± 31.5)	8.6 (± 35.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in percentage of rescue medication-free days

End point title	Changes from baseline in percentage of rescue medication-free days

End point description:

A rescue medication-free day is a day with number of puffs of rescue medication = 0. "Overall" data are reported here

End point type	Secondary

End point timeframe:

Daily, at each clinic visit from Visit 1 to Visit 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: days				
arithmetic mean (standard deviation)	0.28 (± 10.5)	2.24 (± 9.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: ACT scores

End point title	ACT scores

End point description:

The ACT survey is a patient-completed questionnaire with 5 items assessing asthma symptoms (daytime and nocturnal), use of rescue medications, and the effect of asthma on daily functioning. Only data from Visit 5 are reported here.

End point type	Secondary

End point timeframe:

At visits 1, 2 and 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: digit				
arithmetic mean (standard deviation)	22.8 (± 2)	23.1 (± 1.7)		

Statistical analyses

Statistical analysis title	Test treatment vs Reference treatment
Comparison groups	ITT Population - Reference treatment v ITT Population - Test treatment
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.694
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.137

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.827
upper limit	0.553

Secondary: Changes from baseline in heart rate

End point title	Changes from baseline in heart rate

End point description:

Heart rate (HR), systolic and diastolic blood pressure (SBP, DBP) were measured after 10 min rest in sitting position. From visit 2 to visit 5 the measurements were done before the administration of the morning dose of the study drug (pre-dose).

End point type	Secondary

End point timeframe:

At Visit 1 and pre-dose at each clinic visit from Visit 2 to Visit 5

End point values	Safety population - Test treatment	safety population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: beats/min				
arithmetic mean (standard deviation)	-4 (± 9)	-1.2 (± 8.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in systolic blood pressure

End point title	Changes from baseline in systolic blood pressure

End point description:

Heart rate (HR), systolic and diastolic blood pressure (SBP, DBP) were measured after 10 min rest in sitting position. From visit 2 to visit 5 the measurements were done before the administration of the morning dose of the study drug (pre-dose).

End point type	Secondary

End point timeframe:

At Visit 1 and pre-dose at each clinic visit from Visit 2 to Visit 5.

End point values	Safety population - Test treatment	safety population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: mmHg				
arithmetic mean (standard deviation)	-1.2 (± 12.9)	-1.8 (± 13.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in diastolic blood pressure

End point title	Changes from baseline in diastolic blood pressure

End point description:

Heart rate (HR), systolic and diastolic blood pressure (SBP, DBP) were measured after 10 min rest in sitting position. From visit 2 to visit 5 the measurements were done before the administration of the morning dose of the study drug (pre-dose).

End point type	Secondary

End point timeframe:

At Visit 1 and pre-dose at each clinic visit from Visit 2 to Visit 5

End point values	Safety population - Test treatment	safety population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: mmHg				
arithmetic mean (standard deviation)	-0.4 (± 8.8)	-0.6 (± 8.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in average of rescue medication

End point title	Change from baseline in average of rescue medication

End point description:

Use of rescue medication (number of puffs/day) has been calculated as the sum of the number of puffs taken during the day
and during the night. Only "Overall" data are reported here.

End point type	Secondary

End point timeframe:

At Visits 3, 4, and 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: puffs/day				
arithmetic mean (standard deviation)	-0.017 (± 0.223)	-0.054 (± 0.241)		

Statistical analyses

No statistical analyses for this end point

Secondary: Use of concomitant medications to treat asthma exacerbations

End point title	Use of concomitant medications to treat asthma exacerbations

End point description:

End point type	Secondary

End point timeframe:

At Visits 3, 4, and 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: number of subject	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Severe asthma exacerbations

End point title	Severe asthma exacerbations

End point description:

End point type	Secondary

End point timeframe:

At Visits 3, 4, and 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: number of subject	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Unscheduled hospitalizations

End point title	Unscheduled hospitalizations

End point description:

End point type	Secondary

End point timeframe:

At Visits 3, 4, and 5

End point values	ITT Population - Test treatment	ITT Population - Reference treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	54		
Units: number of subject	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events/serious adverse events were measured at each visit, starting from Visit 0 to Visit 5 and to follow-up (phone contact)

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) were reported in the two treatment groups in the safety population.
Treatment-emergent adverse events (TEAEs) = adverse events which occurred after the first intake of the study
medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Safety population - Test treatment

Reporting group description:

Foster® NEXThaler® (beclomethasone dipropionate 100 µg plus formoterol 6 µg per actuation), 2 inhalations b.i.d. (daily dose of BDP 400 µg plus FF 24 µg) plus Seretide® Accuhaler® placebo, 1 inhalation b.i.d.

Reporting group title	Safety population - Reference treatment

Reporting group description:

Seretide Accuhaler: fixed combination of fluticasone propionate 250 µg plus salmeterol xinafoate 50 µg per actuation

Serious adverse events	Safety population - Test treatment	Safety population - Reference treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Safety population - Test treatment	Safety population - Reference treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 54 (25.93%)	10 / 54 (18.52%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 54 (5.56%)	0 / 54 (0.00%)	
occurrences (all)	4	0	
Tachycardia			
subjects affected / exposed	3 / 54 (5.56%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Feeling cold			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Vomiting			

subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
asthma			
subjects affected / exposed	2 / 54 (3.70%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	1 / 54 (1.85%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Influenza			

subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Oral candidiasis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	

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

None reported