Clinical trial results:
A randomized, double-blind, double-dummy, parallel-group, placebo controlled (on inhaled corticosteroid medication), multicenter study to evaluate the efficacy and safety of vilanterol inhalation powder (GW642444) and salmeterol, compared with placebo in the treatment of persistent asthma in adults and adolescents uncontrolled on inhaled corticosteroids.

Summary

EudraCT number	2010-020412-11
Trial protocol	DE Outside EU/EEA
Global end of trial date	26 August 2011

Results information

Result version number	v1 (current)
This version publication date	22 February 2016
First version publication date	27 June 2015

Trial information

Trial identification

Sponsor protocol code	B2C112060

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01181895
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000431-PIP01-08
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	04 October 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the efficacy and safety of vilanterol inhalation powder 25mcg administered once daily in the evening in adolescent and adult subjects 12 years of age and older with persistent asthma over a 12-week treatment period.

Protection of trial subjects:

none

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 110
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Peru: 173
Country: Number of subjects enrolled	Ukraine: 88
Country: Number of subjects enrolled	United States: 147
Worldwide total number of subjects	583
EEA total number of subjects	175

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)	67
Adults (18-64 years)	458

From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

347 participants (par.) were randomized to treatment; all 347 were included in the Intent-to-Treat (ITT) Population. One par. was not randomized but received treatment in error. This par. was not included in the ITT Population and is thus not captured in the Participant Flow module. This par. is categorized as being enrolled in the study (n=348).

Pre-assignment

Screening details:

Participants (par.) meeting eligibility criteria at the Screening visit completed a 28-day Run-in Period for Baseline, safety evaluations, and measures of asthma status. Par. were then randomized to an 8-week Treatment Period. A total of 583 par. were screened, and 347 were randomized, of which 298 completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

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

Dosage and administration details:

once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks

Arm title	Vilanteral 25 µg OD

Arm description:

Participants received Vilanterol (VI) 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Experimental
Investigational medicinal product name	Vilanterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

25 mcg Once daily

Arm title	Salmeterol 50 µg BID

Arm description:

Participants received Salmeterol 50 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Active comparator
Investigational medicinal product name	Salmeterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

50 mcg Twice Daily

Number of subjects in period 1[1]	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID
Started	116	115	116
Completed	99	101	98
Not completed	17	14	18
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	3	-	5
Physician decision	1	2	1
Adverse event, non-fatal	2	1	1
Lost to follow-up	-	1	2
Lack of efficacy	8	9	9
Protocol deviation	2	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 583 participants were screened and enrolled into the study, of these, 347 were randomized to receive study treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.	
Reporting group title	Vilanteral 25 µg OD
Reporting group description:	
Participants received Vilanterol (VI) 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	
Reporting group title	Salmeterol 50 µg BID
Reporting group description:	
Participants received Salmeterol 50 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	

Reporting group values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID
Number of subjects	116	115	116
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	41.7	41	41.1
standard deviation	± 16.64	± 17.81	± 16.84
Gender categorical			
Units: Subjects			
Female	59	68	77
Male	57	47	39
Race, Customized			
Units: Subjects			
African American/African Heritage	11	5	6
American Indian or Alaska Native	37	44	41
Japanese/East Asian Heritage	0	0	1
White	68	66	68

Reporting group values	Total		
Number of subjects	347		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	204		
Male	143		
Race, Customized Units: Subjects			
African American/African Heritage	22		
American Indian or Alaska Native	122		
Japanese/East Asian Heritage	1		
White	202		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

Reporting group title	Vilanteral 25 µg OD

Reporting group description:

Participants received Vilanterol (VI) 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	Salmeterol 50 µg BID

Reporting group description:

Participants received Salmeterol 50 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Primary: Change from Baseline in weighted-mean 24-hour serial forced expiratory volume in one second (FEV1) at Week 12

End point title	Change from Baseline in weighted-mean 24-hour serial forced expiratory volume in one second (FEV1) at Week 12

End point description:

FEV1 is a measure of lung function and is defined as the volume of air that can be forcefully exhaled in one second. The weighted mean is calculated from the pre-dose FEV1 and post-dose FEV1 measurements at 5, 15, and 30 minutes (min) and at 1, 2, 3, 4, 11, 12, 12.5, 13, 14, 16, 20, 23, and 24 hours, respectively, at Week 12. The Baseline value was the Day 1 pre-dose FEV1 measurement. Change from Baseline is calculated as the weighted mean 0-24 hour FEV1 (Liters) at Week 12 minus the Baseline value. Analysis was performed using analysis of covariance (ANCOVA) with covariates of Baseline FEV1, region, sex, age, and treatment. The Intent-to-Treat (ITT) Population was used which includes all participants randomized to treatment who received at least one dose of study medication. Only those participants available at the indicated time point were assessed.

End point type	Primary

End point timeframe:

Baseline and Week 12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95[1]	101[2]	100[3]	
Units: Liters				
least squares mean (standard error)	0.289 (± 0.0429)	0.359 (± 0.0416)	0.283 (± 0.0419)	

Notes:

[1] - ITT Population

[2] - ITT Population

[3] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The estimated value represents the adjusted treatment difference in the weighted mean 0-24 hour FEV1 (Liters) at Week 12 for Vilanterol 25 µg OD versus Placebo.

Comparison groups	Placebo v Vilanteral 25 µg OD
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.244 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.048
upper limit	0.188

Notes:

[4] - P-value for the adjusted treatment difference for Vilanterol 25 µg OD versus Placebo.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The estimated value represents the adjusted treatment difference in the weighted mean 0-24 hour FEV1 (Liters) at Week 12 for Salmeterol 50 µg BID versus Placebo.

Comparison groups	Placebo v Salmeterol 50 µg BID
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.926 [5]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.124
upper limit	0.113

Notes:

[5] - P-value for the adjusted treatment difference for Salmetarol 50 µg BID versus Placebo.

Secondary: Change from Baseline in the percentage of rescue-free 24-hour (hr) periods during the 12-week treatment period

End point title	Change from Baseline in the percentage of rescue-free 24-hour

	(hr) periods during the 12-week treatment period

End point description:

The time span during which the participants did not have to take any rescue bronchodilator (medication intended to relieve symptoms immediately) was considered to be a rescue-free period. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant (including the day of randomization). Change from Baseline is calculated as the value at Weeks 1-12 minus the value at Baseline. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[6]	115[7]	114[8]	
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	14.6 (± 2.71)	21.7 (± 2.68)	22.9 (± 2.72)	

Notes:

[6] - ITT Population. Only those participants available at the indicated time points were assessed.

[7] - ITT Population. Only those participants available at the indicated time points were assessed.

[8] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week treatment period

End point title	Change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week treatment period

End point description:

Participants who were symptom free for 24-hour periods during the12-week treatment period were assessed. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant (including the day of randomization). Change from Baseline is calculated as the value at Weeks 1-12 minus the value at Baseline. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[9]	115[10]	114[11]	
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	12.7 (± 2.58)	19.4 (± 2.55)	19.5 (± 2.59)	

Notes:

[9] - ITT Population. Only those participants available at the indicated time points were assessed.

[10] - ITT Population. Only those participants available at the indicated time points were assessed.

[11] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in individual serial FEV1 assessments at the end of the 12-week treatment period, including the 12-hour and 24-hour time points

End point title	Change from Baseline in individual serial FEV1 assessments at the end of the 12-week treatment period, including the 12-hour and 24-hour time points

End point description:

FEV1 is a measure of lung function and is defined as the volume of air that can be forcefully exhaled in one second. The individual serial FEV1 is calculated from the pre-dose FEV1 and post-dose FEV1 measurements at 5, 15, 30, and 60 minutes (min) and 2, 3, 5, 11, 12, 12.5, 13, 14, 16, 20, 23, and 24 hours, relatively, on Treatment Day 84 (Week 12). The Baseline value was the Day 1 pre-dose FEV1 measurement. Change from Baseline was calculated as the value of the individual serial FEV1 taken at Week 12 minus the Baseline value. Analysis was performed using ANCOVA with covariates of Baseline FEV1, region, sex, age, and treatment. Analysis was performed separately for each planned time point. Only participants available at the specified time points were analyzed(represented by n=X,X,X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116[12]	115[13]	116[14]	
Units: Liters				
least squares mean (standard error)				
Predose, n=97,104,101	0.302 (± 0.0446)	0.272 (± 0.043)	0.233 (± 0.0437)	
5 min, n=95,100,98	0.313 (± 0.045)	0.301 (± 0.0438)	0.214 (± 0.0443)	
15 min, n=96, 101, 99	0.308 (± 0.045)	0.324 (± 0.0439)	0.257 (± 0.0444)	
30 min, n=96,101,100	0.322 (± 0.0443)	0.344 (± 0.0432)	0.272 (± 0.0435)	
60 min, n=96, 101, 100	0.336 (± 0.0445)	0.352 (± 0.0433)	0.296 (± 0.0437)	
2 hours, n=96, 100, 99	0.313 (± 0.0455)	0.369 (± 0.0446)	0.335 (± 0.0449)	
3 hours, n=96, 101, 100	0.304 (± 0.0455)	0.374 (± 0.0444)	0.316 (± 0.0447)	
4 hours, n=96, 101, 100	0.311 (± 0.045)	0.359 (± 0.0438)	0.293 (± 0.0441)	
5 hours, n=96, 100, 100	0.292 (± 0.0455)	0.368 (± 0.0445)	0.279 (± 0.0447)	
11 hours, n=94, 99, 96	0.195 (± 0.0508)	0.312 (± 0.0494)	0.179 (± 0.0505)	

12 hours, n=93,98,95	0.25 (± 0.0477)	0.341 (± 0.0465)	0.217 (± 0.0473)	
12.5 hours, n=96, 97, 98	0.27 (± 0.0446)	0.337 (± 0.0444)	0.282 (± 0.0443)	
13 hours, n= 96, 98, 100	0.312 (± 0.0448)	0.341 (± 0.0442)	0.304 (± 0.044)	
14 hours, n=95, 99, 99	0.341 (± 0.0445)	0.401 (± 0.0436)	0.359 (± 0.0437)	
16 hours, n=95, 98, 97	0.364 (± 0.0464)	0.371 (± 0.0457)	0.357 (± 0.0461)	
20 hours, n= 94, 101, 99	0.318 (± 0.0485)	0.371 (± 0.0467)	0.296 (± 0.0473)	
23 hours, n= 94, 101, 99	0.31 (± 0.0456)	0.345 (± 0.044)	0.271 (± 0.0446)	
24 hours, n= 95, 101, 100	0.301 (± 0.0445)	0.33 (± 0.0432)	0.275 (± 0.0435)	

Notes:

[12] - ITT Population. Only those participants available at the indicated time points were assessed.

[13] - ITT Population. Only those participants available at the indicated time points were assessed.

[14] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily trough (pre-dose and pre-rescue bronchodilator) PM (evening) Peak Expiratory Flow (PEF) averaged over the 12-week treatment period

End point title	Change from Baseline in daily trough (pre-dose and pre-rescue bronchodilator) PM (evening) Peak Expiratory Flow (PEF) averaged over the 12-week treatment period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Trough PEF is the PEF measured approximately 24 hours after the last administration of study drug. The Baseline value is the average value of the last 7 days of daily PM PEF prior to randomization. Change from Baseline in trough PM PEF was calculated as the averaged value of all daily PM PEF for Week 1 to Week 12 minus the value at Baseline. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[15]	115[16]	114[17]	
Units: Liters per minute (L/min)				
least squares mean (standard error)	11 (± 3.15)	24.9 (± 3.14)	18.8 (± 3.17)	

Notes:

[15] - ITT Population. Only those participants available at the indicated time points were assessed.

[16] - ITT Population. Only those participants available at the indicated time points were assessed.

[17] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily AM (morning) PEF averaged over the 12-week treatment period

End point title	Change from Baseline in daily AM (morning) PEF averaged over the 12-week treatment period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Trough PEF is the PEF measured approximately 24 hours after the last administration of study drug. The Baseline value is the average value of the last 7 days of daily AM PEF prior to randomization. Change from Baseline in trough AM PEF was calculated as the averaged value of all daily AM PEF for Weeks 1 to Week 12 minus the value at Baseline. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[18]	115[19]	114[20]	
Units: Liters per minute (L/min)				
least squares mean (standard error)	14.2 (± 3.25)	28 (± 3.24)	23.6 (± 3.27)	

Notes:

[18] - ITT Population. Only those participants available at the indicated time points were assessed.

[19] - ITT Population. Only those participants available at the indicated time points were assessed.

[20] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated time to an increase of >=12% and >=200 milliliters (mL) above Baseline in FEV1 on Day 1 and Day 84 (0-2 hours)

End point title	Number of participants with the indicated time to an increase of >=12% and >=200 milliliters (mL) above Baseline in FEV1 on Day 1 and Day 84 (0-2 hours)

End point description:

The number of participants with a >=12% and >=200 mL increase from Baseline in FEV1 (the maximal amount of air that can be forcefully exhaled in one second) was evaluated on Day 1 and Week 12 for the time to a >=12% increase from Baseline (at the 5 minutes (min), 15 min, 30 min, 1hour (hr), and 2 hr nominal time points. Participants who did not achieve a >=12% and >=200 mL increase from Baseline in FEV1 over this time period were considered censored.

End point type	Secondary

End point timeframe:

Day 1 and Week 12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113[21]	115[22]	116[23]	
Units: Participants				
number (not applicable)				
Day 1, 5 min, n=113, 115, 116	23	33	18	
Day 1, 15 min, n=113, 115, 116	2	11	11	
Day 1, 30 min, n=113, 115, 1116	3	8	13	
Day 1, 1 hr, n=113, 115, 116	3	7	6	
Day 1, 2 hr, n=113, 115, 116	5	6	11	
Day 1, Censored, n=113, 115, 116	77	50	57	
Week 12, 5 min, n=96, 101, 100	39	42	30	
Week 12, 15 min, n=96, 101, 100	6	2	7	
Week 12, 30 min, n=96, 101, 100	2	2	8	
Week 12, 1 hr, n=96, 101, 100	1	4	5	
Week 12, 2 hr, n=96, 101, 100	3	7	4	
Week 12, Censored, n=96, 101, 100	45	44	46	

Notes:

[21] - ITT Population. Only those participants available at the indicated time points were assessed.

[22] - ITT Population. Only those participants available at the indicated time points were assessed.

[23] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Global Assessment of Change questionnaire responses at the end of Week 4 and Week 12

End point title	Number of participants with the indicated Global Assessment of Change questionnaire responses at the end of Week 4 and Week 12

End point description:

At the end of Week 4 and Week 12, the Global Assessment of Change Questionnaire, which assesses changes in asthma symptoms and rescue medication use, was completed by participants using the following scale: asthma symptom (AS) change: much better, somewhat better, a little better, the same, a little worse, somewhat worse, much worse; rescue medication use (RMU): much less often , somewhat less often , a little less often , the same , a little more often , somewhat more often , much more often.

End point type	Secondary

End point timeframe:

Week 4 and Week 12

End point values	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110[24]	109[25]	110[26]	
Units: Participants				
number (not applicable)				
Week 4, AS: Much better, n=110, 109, 110	25	37	34	
Week 4, AS: Somewhat better, n=110, 109, 110	35	43	34	

Week 4, AS: A little better, n=110, 109, 110	24	14	21	
Week 4, AS: The same, n=110, 109, 110	17	13	16	
Week 4, AS: A little worse, n=110, 109, 110	6	1	3	
Week 4, AS: Somewhat worse, n=110, 109, 110	2	0	2	
Week 4, AS: Much worse, n=110, 109, 110	1	1	0	
Week 4, RMU: Much less often, n=110, 109, 110	18	33	28	
Week 4, RMU: Somewhat less often, n=110, 109, 110	40	31	36	
Week 4, RMU: A little less often, n=110, 109, 110	18	23	20	
Week 4, RMU: The same, n=110, 109, 110	26	18	17	
Week 4, RMU: A little more often, n=110, 109, 110	4	3	7	
Week 4, RMU: Somewhat more often, n=110, 109, 110	2	0	2	
Week 4, RMU: Much more often, n=110, 109, 110	2	1	0	
Week 12, AS: Much better, n=100, 105, 101	31	52	35	
Week 12, AS: Somewhat better, n=100, 105, 101	35	31	34	
Week 12, AS: A little better, n=100, 105, 101	13	9	16	
Week 12, AS: The same, n=100, 105, 101	12	9	11	
Week 12, AS: A little worse, n=100, 105, 101	4	2	4	
Week 12, AS: Somewhat worse, n=100, 105, 101	4	1	1	
Week 12, AS: Much worse, n=100, 105, 101	1	1	0	
Week 12, RMU: Much less often, n=100, 105, 101	25	40	32	
Week 12, RMU: Somewhat less often, n=100, 105, 101	31	32	29	
Week 12, RMU: A little less often, n=100, 105, 101	13	16	13	
Week 12, RMU: The same, n=100, 105, 101	23	11	21	
Week 12, RMU: A little more often, n=100, 105, 101	2	5	4	
Week 12, RMU: Somewhat more often, n=100, 105, 101	4	0	2	
Week 12, RMU: Much more often, n=100, 105, 101	2	1	0	

Notes:

[24] - ITT Population. Only those participants available at the indicated time points were assessed.

[25] - ITT Population. Only those participants available at the indicated time points were assessed.

[26] - ITT Population. Only those participants available at the indicated time points were assessed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study treatment until the End-of-Study visit (up to Week 14).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

Reporting group title	Vilanteral 25 µg OD

Reporting group description:

Participants received Vilanterol (VI) 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	Salmeterol 50 µg BID

Reporting group description:

Participants received Salmeterol 50 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 12 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Serious adverse events	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 116 (0.86%)	1 / 115 (0.87%)	0 / 116 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	1 / 116 (0.86%)	0 / 115 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 116 (0.00%)	1 / 115 (0.87%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	Vilanteral 25 µg OD	Salmeterol 50 µg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 116 (22.41%)	26 / 115 (22.61%)	21 / 116 (18.10%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 116 (4.31%)	10 / 115 (8.70%)	9 / 116 (7.76%)
occurrences (all)	8	12	12
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 116 (0.00%)	4 / 115 (3.48%)	1 / 116 (0.86%)
occurrences (all)	0	4	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	7 / 116 (6.03%)	6 / 115 (5.22%)	2 / 116 (1.72%)
occurrences (all)	7	6	2
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 116 (0.00%)	0 / 115 (0.00%)	5 / 116 (4.31%)
occurrences (all)	0	0	6
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 116 (6.90%)	2 / 115 (1.74%)	2 / 116 (1.72%)
occurrences (all)	9	2	2
Nasopharyngitis			
subjects affected / exposed	12 / 116 (10.34%)	9 / 115 (7.83%)	7 / 116 (6.03%)
occurrences (all)	13	10	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2010	The primary purpose of this amendment is to allow more time for requisite site randomization activities between the pre-dose FEV1 and the initial dosing of investigational product at Visit 2. (We increased this to 30 minutes.) Contact information for an additional medical monitor, a correction in the IND Number, and a Table of Clinical Laboratory Tests has also been incorporated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported