



Clinical trial results:

A Randomised, Double-Blind, Double-Dummy, Parallel-Group, Multicentre Study to assess efficacy and safety of Fluticasone Furoate (FF)/GW642444 Inhalation Powder and Fluticasone Propionate (FP) /Salmeterol Inhalation Powder in the Treatment of Persistent Asthma in Adults and Adolescents.

Summary

EudraCT number	2010-019589-10
Trial protocol	NL
Global end of trial date	27 July 2011

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	12 July 2015

Trial information

Trial identification

Sponsor protocol code	HZA113091
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01147848
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, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 September 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the efficacy of FF/GW642444 100/25 mcg, administered once daily in the evening with FP/salmeterol 250/50 mcg administered twice daily in subjects 12 years of age and older with persistent bronchial asthma over a 24 week treatment period.

Protection of trial subjects:

The following steps were taken to protect trial subjects:

- 1). Only subjects meeting all of the inclusion criteria and none of the exclusion criteria were randomized to investigational medication.
- 2). All subjects enrolled into the study were provided rescue medication for use as necessary.
- 3) Both safety and efficacy parameters were also assessed by the investigator regularly in the clinic to minimise any potential risks to the patients.
- 4). The investigator or treating physician may unblind a subject's treatment assignment in the case of an emergency, when knowledge of the study treatment is essential for the appropriate clinical management or welfare of the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 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	Netherlands: 80
Country: Number of subjects enrolled	Argentina: 266
Country: Number of subjects enrolled	Chile: 220
Country: Number of subjects enrolled	Korea, Republic of: 199
Country: Number of subjects enrolled	Philippines: 348
Country: Number of subjects enrolled	United States: 451
Worldwide total number of subjects	1564
EEA total number of subjects	80

Notes:

Subjects enrolled per age group

In utero	0
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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)	130
Adults (18-64 years)	1256
From 65 to 84 years	176
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants ≥ 12 years of age with persistent asthma and Forced Expiratory Volume in one second (FEV1) of 40-85% of predicted normal and airway reversibility demonstrated by increase of $\geq 12\%$ in FEV1 and ≥ 200 ml following 2-4 inhalations of salbutamol/albuterol inhalation aerosol or equivalent dose of nebulised salbutamol/albuterol were eligible.

Period 1

Period 1 title	Run-in Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Fluticasone Propionate 250 µg BID
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Arm description:

Participants received Fluticasone Propionate 250 micrograms (µg) twice a day (BID) and salbutamol/albuterol as required to control symptoms during the Run-In Period. This treatment group was not part of the primary or secondary end point reporting groups.

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

Dosage and administration details:

Participants received Fluticasone Propionate 250 micrograms (µg) twice a day (BID) and salbutamol/albuterol as required to control symptoms.

Number of subjects in period 1	Fluticasone Propionate 250 µg BID
Started	1564
Completed	806
Not completed	758
Screen Failure	623
Run-in Failure	135

Period 2

Period 2 title	Randomized Phase
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Fluticasone Furoate/Vilanterol 100/25 µg OD

Arm description:

Participants received Fluticasone Furoate (FF)/Vilanterol (VI) 100/25 µg once daily (OD) in the evening, plus placebo inhalation powder twice daily (BID; in the morning and evening) for a period of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	FF/VI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

100/25 mcg once daily via Ellipta Device

Arm title	Fluticasone Propionate/Salmeterol 250/50 µg BID
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Arm description:

Participants received Fluticasone Propionate (FP)/Salmeterol 250/50 µg inhalation powder BID (in the morning and evening), plus placebo inhalation powder OD in the evening for a period of 24 weeks.

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

Dosage and administration details:

250/50mcg twice daily via Diskus Inhaler

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline data are reported for participants starting the Randomized Phase (Period 2), which has been denoted as the baseline period.

Number of subjects in period 2^[2]	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID
Started	403	403
Completed	358	357
Not completed	45	46
Consent withdrawn by subject	7	9
Physician decision	-	1
Adverse event, non-fatal	6	8
Lost to follow-up	5	7
Lack of efficacy	20	11
Protocol deviation	7	10

Notes:

[2] - 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: The number of participants enrolled in the trial worldwide (n=1564) represents the number of participants starting the Run-in Phase, not the number starting the Randomized Phase (the baseline period).

Baseline characteristics

Reporting groups

Reporting group title	Fluticasone Furoate/Vilanterol 100/25 µg OD
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Reporting group description:

Participants received Fluticasone Furoate (FF)/Vilanterol (VI) 100/25 µg once daily (OD) in the evening, plus placebo inhalation powder twice daily (BID; in the morning and evening) for a period of 24 weeks.

Reporting group title	Fluticasone Propionate/Salmeterol 250/50 µg BID
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Reporting group description:

Participants received Fluticasone Propionate (FP)/Salmeterol 250/50 µg inhalation powder BID (in the morning and evening), plus placebo inhalation powder OD in the evening for a period of 24 weeks.

Reporting group values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID	Total
Number of subjects	403	403	806
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	43.8	41.9	
standard deviation	± 15.86	± 16.9	-
Gender categorical Units: Subjects			
Female	244	245	489
Male	159	158	317
Race, Customized Units: Subjects			
African American/African Heritage	36	43	79
Asian - Central/South Asian Heritage	1	0	1
Asian - East Asian Heritage	40	46	86
Asian - Japanese Heritage	1	0	1
Asian - South East Asian Heritage	81	79	160
Asian - Mixed Race	1	0	1
Native Hawaiian or Other Pacific Islander	1	1	2
White - Arabic/North African Heritage	1	0	1
White - White/Caucasian/European Heritage	241	232	473
Mixed Race	0	2	2

End points

End points reporting groups

Reporting group title	Fluticasone Propionate 250 µg BID
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Reporting group description:

Participants received Fluticasone Propionate 250 micrograms (µg) twice a day (BID) and salbutamol/albuterol as required to control symptoms during the Run-In Period. This treatment group was not part of the primary or secondary end point reporting groups.

Reporting group title	Fluticasone Furoate/Vilanterol 100/25 µg OD
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Reporting group description:

Participants received Fluticasone Furoate (FF)/Vilanterol (VI) 100/25 µg once daily (OD) in the evening, plus placebo inhalation powder twice daily (BID; in the morning and evening) for a period of 24 weeks.

Reporting group title	Fluticasone Propionate/Salmeterol 250/50 µg BID
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Reporting group description:

Participants received Fluticasone Propionate (FP)/Salmeterol 250/50 µg inhalation powder BID (in the morning and evening), plus placebo inhalation powder OD in the evening for a period of 24 weeks.

Primary: Change from Baseline in weighted-mean 24 hour serial FEV1 on Day 168/Week 24

End point title	Change from Baseline in weighted-mean 24 hour serial FEV1 on Day 168/Week 24
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End point description:

Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. The weighted mean was 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, on Day 168/Week 24. Change from Baseline was calculated as the weighted mean of the 24-hour serial FEV1 measures on Day 168/Week 24 minus the Baseline value. Baseline was the pre-dose measurement on Day 1. Analysis was performed using analysis of covariance (ANCOVA) with covariates of Baseline FEV1, region, sex, age, and treatment. ITT, Intent-to-Treat. Randomized participants were assumed to have received double-blind medication unless definitive evidence to the contrary existed. Only those participants available at the indicated time point were assessed.

End point type	Primary
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End point timeframe:

Baseline and Day 168/Week 24

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	352 ^[1]	347 ^[2]		
Units: Liters				
least squares mean (standard error)	0.341 (± 0.0184)	0.377 (± 0.0185)		

Notes:

[1] - ITT Population: participants randomized to treatment who received ≥1 double-blind medication dose

[2] - ITT Population: participants randomized to treatment who received ≥1 double-blind medication dose

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed using ANCOVA with covariates of Baseline FEV1, region, sex, age, and treatment.	
Comparison groups	Fluticasone Furoate/Vilanterol 100/25 µg OD v Fluticasone Propionate/Salmeterol 250/50 µg BID
Number of subjects included in analysis	699
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.162
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.088
upper limit	0.015

Secondary: Serial FEV1 (0-24 hours)

End point title	Serial FEV1 (0-24 hours)
End point description:	
Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. The pre-dose FEV1 assessment and the individual serial FEV1 assessments at Day 168/Week 24 at the indicated time points (pre-dose, 5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 11 hours, 12 hours, 12.5 hours, 13 hours, 14 hours, 16 hours, 20 hours, 23 hours, and 24 hour s) were summarized.	
End point type	Secondary
End point timeframe:	
Day 168	

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359 ^[3]	354 ^[4]		
Units: Liters				
arithmetic mean (standard deviation)				
Pre-dose, n=359, 353	0.304 (± 0.3575)	0.323 (± 0.4289)		
5 minutes, n=356, 344	0.32 (± 0.3573)	0.339 (± 0.4146)		
15 minutes, n=355, 347	0.323 (± 0.3565)	0.354 (± 0.4054)		
30 minutes, n=357, 351	0.339 (± 0.3614)	0.366 (± 0.4184)		
1 hour, n=358, 353	0.344 (± 0.376)	0.39 (± 0.4227)		

2 hours, n=359, 353	0.362 (± 0.3749)	0.409 (± 0.4204)		
3 hours, n=357, 353	0.373 (± 0.3764)	0.419 (± 0.4173)		
4 hours, n=357, 354	0.356 (± 0.3695)	0.417 (± 0.4254)		
11 hours, n=359, 347	0.305 (± 0.3761)	0.319 (± 0.4099)		
12 hours, n=356, 354	0.33 (± 0.3691)	0.338 (± 0.4142)		
12.5 hours, n=357, 352	0.33 (± 0.3682)	0.38 (± 0.4117)		
13 hours, n=354, 354	0.343 (± 0.3602)	0.396 (± 0.4139)		
14 hours, n=356, 353	0.357 (± 0.3643)	0.426 (± 0.4201)		
16 hours, n=354, 350	0.351 (± 0.3672)	0.419 (± 0.4152)		
20 hours, n=355, 352	0.321 (± 0.3757)	0.376 (± 0.415)		
23 hours, n=354, 353	0.31 (± 0.3814)	0.344 (± 0.4141)		
24 hours, n=354, 354	0.304 (± 0.3725)	0.34 (± 0.4032)		

Notes:

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

[4] - 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 onset of bronchodilator effect at Day 1

End point title	Number of participants with the indicated time to onset of bronchodilator effect at Day 1
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End point description:

Time to onset of bronchodilator effect at Day 1 is defined as the actual time during the 4-hour serial FEV1 (the maximal amount of air that can be forcefully exhaled in one second) measurements that the participant first meets or exceeds a 12% and 200 mL increase over Baseline and was derived at Day 1 only. Time to onset was calculated over 0 to 4 hours (5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3 hours, and 4 hours) post-dose. Participants who never exceeded a 12% and 200 mL increase over Baseline were censored at the actual time of their last FEV1 measurement.

End point type	Secondary
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End point timeframe:

Baseline to Day 1

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400 ^[5]	401 ^[6]		
Units: participants				
5 minutes	100	85		
15 minutes	41	51		

30 minutes	40	55		
1 hour	32	39		
2 hours	19	29		
3 hours	17	12		
4 hours	11	12		
Censored	140	118		

Notes:

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

[6] - 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 weighted mean serial FEV1 over 0-4 hours post first dose (at Randomization)

End point title	Change from Baseline in weighted mean serial FEV1 over 0-4 hours post first dose (at Randomization)
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End point description:

The weighted mean serial FEV1 (the maximal amount of air that can be forcefully exhaled in one second) over 0-4 hours post-dose at Baseline was derived using actual times and using the pre-dose assessment as the 0 hour measurement. Change from Baseline was calculated as the weighted mean of the 4-hour serial FEV1 measures on Day 1 minus the Baseline value. Baseline was the pre-dose measurement on Day 1. Analysis was performed using ANCOVA with covariates of Baseline FEV1, region, sex, age, and treatment.

End point type	Secondary
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End point timeframe:

Baseline and Randomization

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	398 ^[7]	398 ^[8]		
Units: Liters				
least squares mean (standard error)	0.316 (± 0.0149)	0.346 (± 0.0149)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in weighted mean serial FEV1 over 0-4 hours at Day 168

End point title	Change from Baseline in weighted mean serial FEV1 over 0-4 hours at Day 168
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End point description:

The weighted mean serial FEV1 (the maximal amount of air that can be forcefully exhaled in one second) over 0-4 hours post-dose at Baseline and Day 168 was derived using actual times and using the

pre-dose assessment as the 0 hour measurement. Change from Baseline was calculated as the weighted mean of the 4-hour serial FEV1 measures on Day 168/Week 24 minus the Baseline value. Baseline was the pre-dose measurement on Day 1. Analysis was performed using ANCOVA with covariates of Baseline FEV1, region, sex, age, and treatment.

End point type	Secondary
End point timeframe: Baseline and Day 168	

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356 ^[9]	347 ^[10]		
Units: Liters				
arithmetic mean (standard deviation)	0.36 (± 0.0184)	0.394 (± 0.0186)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants obtaining a $\geq 12\%$ and ≥ 200 mL increase from Baseline in FEV1 at 12 hours and at 24 hours

End point title	Number of participants obtaining a $\geq 12\%$ and ≥ 200 mL increase from Baseline in FEV1 at 12 hours and at 24 hours
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End point description:

The number of participants obtaining a $\geq 12\%$ and ≥ 200 mL increase from Baseline in FEV1 (the maximal amount of air that can be forcefully exhaled in one second) was evaluated at 12-hours post-dose and at 24-hours post-dose on Day 168.

End point type	Secondary
End point timeframe: Baseline and Day 168	

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356 ^[11]	354 ^[12]		
Units: participants				
12 hours post-dose, n=356, 354	199	178		
24 hours post-dose, n=354, 354	181	176		

Notes:

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

[12] - 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 Trough FEV1 at Day 168

End point title Change from Baseline in Trough FEV1 at Day 168

End point description:

Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 is defined as the pre-dose measurement on Day 168/Week 24. Any missing data at Day 168/Week 24 was imputed using the last observation carried forward (LOCF). Baseline was the pre-dose measurement on Day 1. Change from Baseline was calculated as the pre-dose measurement on Day 168/Week 24 minus the Baseline value.

End point type Secondary

End point timeframe:

Baseline and Day 168

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	397 ^[13]	389 ^[14]		
Units: Liters				
least squares mean (standard error)	0.281 (± 0.0191)	0.3 (± 0.0193)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Asthma Control Test (ACT) scores at Day 168

End point title Change from Baseline in Asthma Control Test (ACT) scores at Day 168

End point description:

The ACT is a 5-item questionnaire developed as a measure of the participant's asthma control. Questions are designed to be self-completed by the participant and include the following: "In the past 4 weeks, "How much of the time did your asthma keep you from getting as much done at work, school or at home?", "How often have you had shortness of breath?", "How often did your asthma symptoms wake you up at night or earlier than usual in the morning?", "How often have you used your rescue inhaler or nebulizer medication (such as albuterol)?" and "How would you rate your asthma control"? The ACT total score is defined as the sum of the scores from all 5 questions, provided all questions have been answered; thus, the total score ranges from 5 (poor control of asthma) to 25 (complete control of asthma). A score of 20 or higher indicates well-controlled asthma. Change from Baseline was calculated as the Day 168 value minus the Baseline value.

End point type Other pre-specified

End point timeframe:

Baseline and Day 168

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	354 ^[15]	348 ^[16]		
Units: Scores on a scale				
least squares mean (standard error)	2.3 (± 0.16)	2 (± 0.16)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of healthcare contacts related to asthma or the treatment of asthma from Baseline to Day 168

End point title	Number of healthcare contacts related to asthma or the treatment of asthma from Baseline to Day 168
End point description:	All unscheduled asthma-related visits to a physician's office, visits to urgent care, visits to the emergency department, and hospitalizations (to the general ward [GW] or the intensive care unit [ICU]) that were associated with asthma exacerbations were recorded.
End point type	Other pre-specified
End point timeframe:	Baseline to Day 168

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403 ^[17]	403 ^[18]		
Units: visits per participant				
arithmetic mean (standard deviation)				
Number of Home Visits during the Day	0 (± 0)	0 (± 0.05)		
Number of Home Visits during the Night	0 (± 0)	0 (± 0)		
Number of Physician Office/Practice Visits	0 (± 0.29)	0 (± 0.18)		
Number of Urgent Care/Outpatient Clinic Visits	0 (± 0.05)	0 (± 0.05)		
Number of Emergency Room Visits	0 (± 0.15)	0 (± 0.14)		
Number of Inpatient Hospitalization (ICU) Days	0 (± 0)	0 (± 0)		
Number of Inpatient Hospitalization (GW) Days	0 (± 0.2)	0 (± 0.39)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Asthma Quality of Life Questionnaire (AQLQ) total score for participants 12 years of age and older (AQLQ + 12)

End point title	Change from Baseline in Asthma Quality of Life Questionnaire (AQLQ) total score for participants 12 years of age and older (AQLQ + 12)
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End point description:

The AQLQ is a disease-specific, self-administered quality of life (QOL) questionnaire developed to evaluate the impact of asthma treatments on the QOL of asthma sufferers. The AQLQ contains 32 items in four domains: activity limitation (11 items), symptoms (12 items), emotional function (5 items), and environmental stimuli (4 items). The response format consists of a 7-point scale: a value of 1 indicates "total impairment"; a value of 7 indicates "no impairment." The AQLQ total score is defined as the average of the scores from all 32 questions, provided at least 90% of the questions have been answered; thus, the total score ranges from 1 (indicates "total impairment") to 7 (indicates "no impairment"). Change from Baseline was calculated as the Day 168 value minus the Baseline value. Analysis was performed using ANCOVA with covariates of Baseline total AQLQ score, country, sex, age, and treatment.

End point type	Other pre-specified
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End point timeframe:

Baseline and Day 168

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342 ^[19]	335 ^[20]		
Units: Scores on a scale				
least squares mean (standard error)	0.46 (± 0.043)	0.37 (± 0.043)		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of participants with "No Problems" in the EQ-5D Descriptive System Dimensions at Day 168/Week 24

End point title	Percentage of participants with "No Problems" in the EQ-5D Descriptive System Dimensions at Day 168/Week 24
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End point description:

The EuroQol five-dimensions (EQ-5D) is a standardized, 2-part, self-assessment instrument, designed for self-completion, used to measure health outcome. The first part consists of 5 items covering 5 dimensions (mobility, self care, usual activities, pain/discomfort, and anxiety/depression). Each dimension is measured by a three-point Likert scale (1=no problems, 2=some problems and 3=severe problems). Respondents are asked to choose one level that reflects their "own health state today" for each of the five dimensions.

End point type	Other pre-specified
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End point timeframe:

Day 168/Week 24

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403 ^[21]	403 ^[22]		
Units: participants	86	84		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in EQ-5D Visual Analog Scale (VAS) Score at Day 168

End point title	Change from Baseline in EQ-5D Visual Analog Scale (VAS) Score at Day 168
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End point description:

The EQ-5D is a standardized, 2-part, self-assessment instrument, designed for self-completion, used to measure health outcome. The first part consists of 5 items covering 5 dimensions (mobility, self care, usual activities, pain/discomfort, and anxiety/depression). The second part is a 20 centimeter VAS that has endpoints labelled "best imaginable health state" and "worst imaginable health state" anchored at 100 and 0, respectively. Participants were asked to indicate how they rate their own health by drawing a line from an anchor box to that point on the EQ-VAS that best represents their own health on that day. Analysis was performed using ANCOVA with covariates of Baseline VAS score, country, sex, age, and treatment.

End point type	Other pre-specified
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End point timeframe:

Baseline and Day 168

End point values	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343 ^[23]	349 ^[24]		
Units: scores on a scale				
least squares mean (standard error)	5.5 (± 0.6)	4.1 (± 0.6)		

Notes:

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

[24] - ITT Population. Only those participants available at the indicated time point 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 the study medication until Follow-up (up to 544 days).

Adverse event reporting additional description:

All AEs and SAEs were followed until resolution, until the condition stabilized, until the event was otherwise explained, or until the participant was lost to follow-up.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	Fluticasone Furoate/Vilanterol 100/25 µg OD
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Reporting group description:

Participants received Fluticasone Furoate (FF)/Vilanterol (VI) 100/25 µg once daily (OD) in the evening, plus placebo inhalation powder twice daily (BID; in the morning and evening) for a period of 24 weeks.

Reporting group title	Fluticasone Propionate/Salmeterol 250/50 µg BID
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Reporting group description:

Participants received Fluticasone Propionate (FP)/Salmeterol 250/50 µg inhalation powder BID (in the morning and evening), plus placebo inhalation powder OD in the evening for a period of 24 weeks.

Serious adverse events	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 403 (0.99%)	5 / 403 (1.24%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed	0 / 403 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	1 / 403 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 403 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 403 (0.25%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 403 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 403 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 403 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 403 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fluticasone Furoate/Vilanterol 100/25 µg OD	Fluticasone Propionate/Salmeterol 250/50 µg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 403 (27.30%)	106 / 403 (26.30%)	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	34 / 403 (8.44%) 42	41 / 403 (10.17%) 74	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	13 / 403 (3.23%) 14	5 / 403 (1.24%) 5	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	15 / 403 (3.72%) 21	13 / 403 (3.23%) 15	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	25 / 403 (6.20%) 33 46 / 403 (11.41%) 52	16 / 403 (3.97%) 16 46 / 403 (11.41%) 63	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2010	SCOPE: This amendment applies to all sites. <ul style="list-style-type: none"><li data-bbox="418 389 1414 450">• To amend the pre-dose FEV1 assessment at randomisation (Visit 2) from 5 minutes to within 30 minutes of dosing;<li data-bbox="418 450 1414 510">• To insert a serum pregnancy test for females of child-bearing potential at early Withdrawal Visit on the Time and Events Table.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported