Clinical trial results:
A Long-Term, Randomized, Double-Blind, Parallel Group Study of Fluticasone Furoate/GW642444 Inhalation Powder Once-Daily and Fluticasone Furoate Inhalation Powder Once- Daily in Subjects with Asthma

Summary

EudraCT number	2009-011461-84
Trial protocol	DE Outside EU/EEA
Global end of trial date	15 September 2011

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	09 February 2015

Trial information

Trial identification

Sponsor protocol code	HZA106837

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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)	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	24 November 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate that treatment with Fluticasone Furoate/GW642444 Inhalation Powder once-daily administered in the evening significantly decreased the risk of severe asthma exacerbations as measured by time to first severe asthma exacerbation when compared with the same dose of Fluticasone Furoate Inhalation Powder alone administered once-daily in the evening in subjects 12 years of age and older with asthma. This study will establish the safety as well as demonstrate benefit of the addition of a LABA to an ICS by utilizing an endpoint (time to first severe asthma exacerbation) that informs on both safety and efficacy.

Protection of trial subjects:

Participants with life-threatening asthma were not enrolled in the study. Withdrawal of the participant from the trial was required if any of the following criteria were met: participant experienced three severe asthma exacerbations in any 6-month period or four severe asthma exacerbations during the double-blind treatment period; participant became pregnant; participant had an adverse event that would make continued participation in the study an unacceptable risk (in the judgment of the investigator); or liver chemistry threshold criteria were met. An Independent Data Monitoring Committee was utilized to ensure external objective medical and/or statistical review of safety and/or efficacy issues in order to protect the ethical and safety interests of the participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 187
Country: Number of subjects enrolled	Romania: 176
Country: Number of subjects enrolled	Germany: 236
Country: Number of subjects enrolled	Argentina: 187
Country: Number of subjects enrolled	Australia: 60
Country: Number of subjects enrolled	Philippines: 184
Country: Number of subjects enrolled	Russian Federation: 354
Country: Number of subjects enrolled	Mexico: 264
Country: Number of subjects enrolled	Ukraine: 238
Country: Number of subjects enrolled	Japan: 125
Country: Number of subjects enrolled	United States: 657
Worldwide total number of subjects	2668
EEA total number of subjects	599

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)	344
Adults (18-64 years)	2102
From 65 to 84 years	220
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants (par.) who met all entry criteria at Screening entered a 2-week Run-in Period for completion of Baseline safety evaluations and to obtain Baseline measures of asthma status. Participants who met continuation criteria at the end of the Run-in Period were randomized to receive study treatment.

Period 1

Period 1 title	2-week Run-in Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	FP 250 µg/ICS

Arm description:

Japanese participants using fluticasone propionate (FP)/salmeterol 250/50 micrograms (µg) twice daily received open-label FP 250 µg to ensure they continued their inhaled corticosteroid (ICS) therapy at a fixed dose during the 2-week Run-in Period. All other participants continued to use their current ICS therapy at a fixed dose during the 2-week Run-in Period. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Run-in Period.

Arm type	Unblinded run-in medication
Investigational medicinal product name	fluticasone propionate (FP) 250 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

250 µg, twice daily

Number of subjects in period 1	FP 250 µg/ICS
Started	2183
Completed	2020
Not completed	163
Physician decision	6
Consent withdrawn by subject	19
Adverse event, non-fatal	1
Continuation Criteria Not Met	92
Lost to follow-up	1
Study Closed/Terminated	42
Protocol deviation	1
Randomized in Error	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FF 100 µg

Arm description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a dry powder inhaler (DPI) once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

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

Dosage and administration details:

100 micrograms (µg), once daily in the evening

Arm title	FF/VI 100/25 µg

Arm description:

Participants received FF/vilanterol (VI) 100/25 µg inhalation powder via a DPI once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Fluticasone furoate/vilanterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

100/25 µg, once daily in the evening

Notes:

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

Justification: The randomized treatment period is considered to be the baseline period. Subject disposition data are collected for members of the Intent-to-Treat Population, defined as all randomized participants who received at least a single dose of trial medication. Not all participants enrolled in the trial (participants screened and for whom a record exists on the study database) were randomized to treatment.

Number of subjects in period 2[2][3]	FF 100 µg	FF/VI 100/25 µg
Started	1010	1009
Intent-to-Treat (ITT) Population	1010	1009
Completed	863	885
Not completed	147	124
Consent withdrawn by subject	53	55
Physician decision	9	6
Adverse event, non-fatal	19	15
Lost to follow-up	11	9
Study Closed/Terminated	7	8
Protocol deviation	26	17
Lack of efficacy	22	13
Protocol-Defined Stopping Criteria	-	1

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: Subject disposition data are collected for members of the Intent-to-Treat Population, defined as all randomized participants who received at least a single dose of trial medication. Not all participants enrolled in the trial (participants screened and for whom a record exists on the study database) were randomized to treatment.

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One participant who completed the 2-week Run-in Period was not randomised but recieved treatment (fluticasone furoate 100 micrograms) in error. This participant is not included in the Intent-to-Treat (ITT) population. Only those participants comprising the ITT Population started the Treatment Period.

Baseline characteristics

Reporting groups	
Reporting group title	FF 100 µg
Reporting group description:	
Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a dry powder inhaler (DPI) once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.	
Reporting group title	FF/VI 100/25 µg
Reporting group description:	
Participants received FF/vilanterol (VI) 100/25 µg inhalation powder via a DPI once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.	

Reporting group values	FF 100 µg	FF/VI 100/25 µg	Total
Number of subjects	1010	1009	2019
Age categorical			
Units: Subjects			
Age continuous			
Baseline characteristic data were collected in members of the Intent-to-Treat Population, comprised of all participants randomized to treatment who received at least one dose of study medication.			
Units: years			
arithmetic mean	42.3	41.1	
standard deviation	± 16.82	± 17.1	-
Gender categorical			
Baseline characteristic data were collected in members of the Intent-to-Treat Population, comprised of all participants randomized to treatment who received at least one dose of study medication.			
Units: Subjects			
Female	689	661	1350
Male	321	348	669
Race, customized			
Baseline characteristic data were collected in members of the Intent-to-Treat Population, comprised of all participants randomized to treatment who received at least one dose of study medication.			
Units: Subjects			
African American/African Heritage	47	40	87
American Indian or Alaska Native	4	9	13
Asian - Central/South Asian Heritage	0	2	2
Asian - East Asian Heritage	1	0	1
Asian - Japanese Heritage	30	32	62
Asian - South East Asian Heritage	79	78	157
Native Hawaiian or other Pacific Islander	2	0	2
White - Arabic/North African Heritage	5	2	7
White - White/Caucasian/European Heritage	738	738	1476
Mixed Race	104	108	212

End points

End points reporting groups

Reporting group title	FP 250 µg/ICS

Reporting group description:

Japanese participants using fluticasone propionate (FP)/salmeterol 250/50 micrograms (µg) twice daily received open-label FP 250 µg to ensure they continued their inhaled corticosteroid (ICS) therapy at a fixed dose during the 2-week Run-in Period. All other participants continued to use their current ICS therapy at a fixed dose during the 2-week Run-in Period. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Run-in Period.

Reporting group title	FF 100 µg

Reporting group description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a dry powder inhaler (DPI) once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

Reporting group title	FF/VI 100/25 µg

Reporting group description:

Participants received FF/vilanterol (VI) 100/25 µg inhalation powder via a DPI once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

Primary: Number of participants with 1 or more severe asthma exacerbations

End point title	Number of participants with 1 or more severe asthma exacerbations

End point description:

Asthma is a medical condition that causes narrowing of the small airways in the lungs. A severe asthma exacerbation is defined as a deterioration of asthma requiring the use of systemic corticosteroids (tablets, suspension, or injection) for at least 3 days or an in-patient hospitalization or emergency department visit due to asthma that required systemic corticosteroids. Only events deemed by the adjudication committee to be severe asthma exacerbations were used in the analysis of severe asthma exacerbations. The time to the first severe asthma exacerbation was analyzed using a Cox proportional hazards regression model, adjusting for Baseline disease severity (Baseline forced expiratory volume in one second [FEV1, maximum amount of air forcefully exhaled in one second]), sex, age, and region.

End point type	Primary

End point timeframe:

Baseline to Follow-up (up to 76 weeks of treatment)

End point values	FF 100 µg	FF/VI 100/25 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1010[1]	1009[2]		
Units: participants	186	154		

Notes:

[1] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication
[2] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication

Statistical analyses

Statistical analysis title	Statistical Analysis #1
Comparison groups	FF/VI 100/25 µg v FF 100 µg
Number of subjects included in analysis	2019
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Regression Cox
Point estimate	0.795
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.642
upper limit	0.985

Notes:

[3] - The estimated values is the Hazard ratio obtained from the Cox regression analysis for FF/VI 100/25 µg versus FF 100 µg, adjusted for an interim analysis.

Statistical analysis title	Statistical Analysis #2

Statistical analysis description:

The estimated value represents the adjusted probability of 1 or more severe asthma exacerbations by Week 52 for FF 100 µg. Cox Proportional Hazards Model estimate at mean Baseline FEV1, age, and proportional coefficients for sex and region.

Comparison groups	FF/VI 100/25 µg v FF 100 µg
Number of subjects included in analysis	2019
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [4]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.5
upper limit	18.2

Notes:

[4] - P-value for the Hazard ratio obtained from the Cox regression analysis for FF/VI 100/25 µg versus FF 100 µg, adjusted for an interim analysis.

Statistical analysis title	Statistical Analysis #3

Statistical analysis description:

The estimated value represents the adjusted probability of 1 or more severe asthma exacerbations by Week 52 for FF/VI 100/25 µg. Cox Proportional Hazards Model estimate at mean Baseline FEV1, age, and proportional coefficients for sex and region.

Comparison groups	FF/VI 100/25 µg v FF 100 µg
Number of subjects included in analysis	2019
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [5]
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	12.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	10.7
upper limit	14.9

Notes:

[5] - P-value for the Hazard ratio obtained from the Cox regression analysis for FF/VI 100/25 µg versus FF 100 µg, adjusted for an interim analysis.

Secondary: Number of severe asthma exacerbations

End point title	Number of severe asthma exacerbations

End point description:

A severe asthma exacerbation is defined as a deterioration of asthma requiring the use of systemic corticosteroids (tablets, suspension, or injection) for at least 3 days or an in-patient hospitalization or emergency department visit due to asthma that required systemic corticosteroids. A participant may have had one or more exacerbations.

End point type	Secondary

End point timeframe:

Baseline to Follow-up (up to 76 weeks of treatment)

End point values	FF 100 µg	FF/VI 100/25 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1010[6]	1009[7]		
Units: Severe asthma exacerbations	271	200		

Notes:

[6] - ITT Population

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in evening pre-dose trough FEV1 at Week 36

End point title	Change from Baseline in evening pre-dose trough FEV1 at Week 36

End point description:

Evening pre-dose trough (lowest value) forced expiratory volume in one second (FEV1) was measured using spirometry equipment that met or exceeded the minimal performance recommendations of the American Thoracic Society. FEV1 is a measure of the maximum amount of air forcefully exhaled in one second. Change from Baseline in evening pre-dose FEV1 was analyzed using an Analysis of Covariance (ANCOVA) model with effects due to Baseline FEV1, sex, age, region, and treatment. Change from Baseline was calculated as the Week 36 value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Week 36

End point values	FF 100 µg	FF/VI 100/25 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	902[8]	926[9]		
Units: Liters				
least squares mean (standard error)	0.265 (± 0.014)	0.348 (± 0.014)		

Notes:

[8] - ITT Population. Only participants available at the indicated time point (Week 36) were analyzed.

[9] - ITT Population. Only participants available at the indicated time point (Week 36) were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to End of Study

Adverse event reporting additional description:

Serious adverse events (SAEs) and non-serious AEs are reported for members of the ITT Population, comprised of all participants randomized to treatment who received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	FF 100 µg

Reporting group description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a dry powder inhaler (DPI) once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

Reporting group title	FF/VI 100/25 µg

Reporting group description:

Participants received FF/vilanterol (VI) 100/25 µg inhalation powder via a DPI once daily in the evening. Short-acting beta2-agonist inhalation aerosol (albuterol/salbutamol) was provided to be used as needed for symptomatic relief of asthma symptoms during the Treatment Period.

Serious adverse events	FF 100 µg	FF/VI 100/25 µg	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 1010 (2.87%)	41 / 1009 (4.06%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondroma			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer stage I			

subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 1010 (0.10%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Diabetic microangiopathy			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 1010 (0.10%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Dysfunctional uterine bleeding			

subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (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			
Nasal polyps			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	9 / 1010 (0.89%)	11 / 1009 (1.09%)	
occurrences causally related to treatment / all	1 / 10	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fear			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Upper limb fracture			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 1010 (0.10%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			

subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocholecystis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			

subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 1010 (0.00%)	1 / 1009 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 1010 (0.40%)	4 / 1009 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Diabetic foot			
subjects affected / exposed	1 / 1010 (0.10%)	0 / 1009 (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: 3 %

Non-serious adverse events	FF 100 µg	FF/VI 100/25 µg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	479 / 1010 (47.43%)	467 / 1009 (46.28%)	
Nervous system disorders			
Headache			
subjects affected / exposed	179 / 1010 (17.72%)	188 / 1009 (18.63%)	
occurrences (all)	599	615	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	23 / 1010 (2.28%)	36 / 1009 (3.57%)	
occurrences (all)	29	48	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	26 / 1010 (2.57%)	33 / 1009 (3.27%)	
occurrences (all)	41	97	
Rhinitis allergic			
subjects affected / exposed	26 / 1010 (2.57%)	39 / 1009 (3.87%)	
occurrences (all)	31	58	
Oropharyngeal pain			
subjects affected / exposed	55 / 1010 (5.45%)	41 / 1009 (4.06%)	
occurrences (all)	63	57	
Cough			
subjects affected / exposed	64 / 1010 (6.34%)	55 / 1009 (5.45%)	
occurrences (all)	95	89	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	40 / 1010 (3.96%)	41 / 1009 (4.06%)	
occurrences (all)	58	52	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	41 / 1010 (4.06%)	29 / 1009 (2.87%)	
occurrences (all)	45	32	
Sinusitis			

subjects affected / exposed	38 / 1010 (3.76%)	42 / 1009 (4.16%)	
occurrences (all)	55	67	
Influenza			
subjects affected / exposed	38 / 1010 (3.76%)	50 / 1009 (4.96%)	
occurrences (all)	48	60	
Bronchitis			
subjects affected / exposed	74 / 1010 (7.33%)	59 / 1009 (5.85%)	
occurrences (all)	85	75	
Upper respiratory tract infection			
subjects affected / exposed	93 / 1010 (9.21%)	73 / 1009 (7.23%)	
occurrences (all)	129	114	
Nasopharyngitis			
subjects affected / exposed	131 / 1010 (12.97%)	155 / 1009 (15.36%)	
occurrences (all)	194	247	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2009	Japanese country-specific amendment to: change age of eligible participants to 18 years of age and older; addition of open-label fluticasone propionate 250 µg for use by appropriate participants during the 2-week Run-in Period; addition of clinical laboratory testing at Weeks 12, 28, and 52 and last on-treatment visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported