Protocol Registration Receipt
07/24/2014

Grantor: CDER IND/IDE Number: 077855 & 050703 Serial Number:

A Study to Assess the Efficacy of Fluticasone Furoate/Vilanterol (FF/VI) Inhalation Powder 100/25 mcg Once Daily Compared With Fluticasone Propionate/Salmeterol Inhalation Powder 250/50 mcg Twice Daily in Subjects With Chronic Obstructive Pulmonary Disease (COPD)

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT01706328

Purpose

This will be a Phase IIIb multicentre, randomized, double-blind, double-dummy, 12-week parallel group study evaluating the effects of once daily in the morning treatment of FF/VI Inhalation Powder versus Fluticasone Propionate/Salmeterol Inhalation Powder twice daily on lung function in COPD subjects.

Subjects will be screened and will enter a 2-week, single-blind (placebo), Run-In Period to evaluate the subject's adherence with study treatment, study procedures and assessment of disease stability.

At the end of the Run-In Period, subjects will return to the Clinic and who meet all of the Randomization Criteria will be randomized to double-blind study medication (12-week treatment period). Subjects will be randomized to receive either FF/VI 100/25 via NDPI or Fluticasone Propionate/Salmeterol 250/50mcg via ACCUHALER/DISKUS. Matching placebos will be available in NDPI and ACCUHALER/DISKUS. Each morning (approximately 6-10 AM) subjects will take 1 inhalation from the NDPI followed by 1 inhalation from the ACCUHALER/DISKUS. Each evening (approximately 6-10 PM), approximately 12 hours after the morning dose with blinded study medication, subjects will take 1 inhalation from the ACCUHALER/DISKUS. Subjects will return to the clinic at the end of the treatment period.

A follow-up phone contact will be performed approximately 7 days after the last clinic visit. The overall study duration (Screening to Follow-up) for each subject is approximately 15 weeks.

Condition	Intervention	Phase
Pulmonary Disease, Chronic Obstructive	Drug: FF/VI 100/25 Inhalation Powder NDPI Drug: Fluticasone Propionate/Salmeterol 250/50 Inhalation Powder ACCUHALER/DISKUS Drug: Placebo Inhalation Powder NDPI Drug: Placebo Inhalation Powder ACCUHALER/DISKUS Drug: Salbutamol as needed	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Efficacy Study
Official Title: A 12-Week Study to Evaluate the 24-Hour Pulmonary Function Profile of Fluticasone Furoate/Vilanterol (FF/VI) Inhalation Powder 100/25 mcg Once Daily Compared With Fluticasone Propionate/Salmeterol Inhalation Powder 250/50 mcg Twice Daily in Subjects With Chronic Obstructive Pulmonary Disease (COPD)

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Change From Baseline Trough in Weighted-mean 24-hour Serial Forced Expiratory Volume in One Second (FEV1) on Treatment Day 84 [Time Frame: Baseline and Day 84] [Designated as safety issue: No]

  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 was calculated from the pre-dose FEV1 and the post-dose FEV1 measurements taken at 5, 15, 30, and 60 minutes and 2, 4, 6, 8, 12, 13, 14, 16, 20, and 24 hours on Treatment Day 84. Baseline trough FEV1 was calculated as the mean of the two assessments made 30 minutes pre-dose and 5 minutes pre-dose on

Treatment Day 1. The weighted mean was derived by calculating the area under curve, and then dividing by the relevant time interval. The weighted mean change from Baseline was calculated as the weighted mean of the 24-hour serial FEV1 measurements on Day 84 minus the Baseline trough FEV1 value. The analysis used an analysis of covariance (ANCOVA) model with covariates of Baseline FEV1, reversibility stratum, smoking status (at Screening), country, and treatment.

Secondary Outcome Measures:

- Time to Onset on Treatment Day 1 [Time Frame: Baseline and Day 1] [Designated as safety issue: No]
  Time to onset on Treatment Day 1 is defined as the time to an increase of 100 milliliters (mL) from Baseline in FEV1 during the 0- to 4-hour serial measurements (5, 15, 30, 60, 120, and 240 minutes post-dose). Participants who never met or exceeded a 100 mL increase over the Baseline value during the 4-hour serial measurements were censored at the actual time of their last FEV1 measurement.
- Change From Baseline in Trough FEV1 on Treatment Day 85 [Time Frame: Baseline and Day 85] [Designated as safety issue: No]
  FEV1 is a measure of lung function and is defined as the volume of air that can be forcefully exhaled in one second. Trough FEV1 is defined as the 24-hour FEV1 assessment, which was obtained on Day 85. Baseline trough was calculated as the mean of the two assessments made 30 minutes pre-dose and 5 minutes pre-dose on Treatment Day 1. Change from Baseline was calculated as the average of the Day 85 values minus the Baseline value. The analysis used an analysis of covariance (ANCOVA) model with covariates of Baseline FEV1, reversibility stratum, smoking status (at Screening), country, and treatment.

Enrollment: 828
Study Start Date: October 2012
Study Completion Date: June 2013
Primary Completion Date: June 2013

Arms	Assigned Interventions
Experimental: FF/VI Inhalation Powder NDPI Subjects randomized to the FF/VI 100/25 arm will take an active inhalation of study medication during their morning dosing from their NDPI and will have an inhalation of dummy medication (placebo) as their morning ACCUHALER/DISKUS dose and as their evening dose.	Drug: FF/VI 100/25 Inhalation Powder NDPI Subjects randomized to the FF/VI Inhalation Powder Novel Dry Powder Inhaler (NDPI) arm will receive a single inhalation of 100 mcg FF and 25 mcg VI via NDPI every morning for 12 weeks. Drug: Placebo Inhalation Powder ACCUHALER/DISKUS Subjects randomized to the FF/VI Inhalation Powder NDPI arm will receive a single inhalation of placebo inhalation powder via ACCUHALER/DISKUS once in the morning and once in the evening for 12 weeks.

Arms	Assigned Interventions
	Drug: Salbutamol as needed Salbutamol inhalation powder
Active Comparator: Fluticasone Propionate/Salmeterol Inhalation Powder Subjects randomized to the Fluticasone Propionate/Salmeterol Inhalation Powder 250/50mcg arm will have an active dose of medication during both their morning and evening treatments from the ACCUHALER/DISKUS and a dummy placebo dose in the morning from their NDPI.	Drug: Fluticasone Propionate/Salmeterol 250/50 Inhalation Powder ACCUHALER/DISKUS Subjects randomized to the Fluticasone Propionate/Salmeterol Inhalation Powder ACCUHALER/DISKUS arm will receive a single inhalation of 250 mcg Fluticasone Propionate and 50 mcg Salmeterol via ACCUHALER/DISKUS once in the morning and once in the evening for 12 weeks. Other Names: ACCUHALER and DISKUS are registered trade marks of the GlaxoSmithKline Group of companies Drug: Placebo Inhalation Powder NDPI Subjects randomized to the Fluticasone Propionate/Salmeterol Inhalation Powder ACCUHALER/DISKUS arm will receive a single inhalation of placebo inhalation powder via NDPI every morning for 12 weeks. Other Names: ACCUHALER and DISKUS are registered trade marks of the GlaxoSmithKline Group of companies Drug: Salbutamol as needed Salbutamol inhalation powder

Eligibility

Ages Eligible for Study: 40 Years and older

Genders Eligible for Study: Both

Inclusion Criteria:

- A male or female >=40 years of age at Screening (Visit 1).
- Capable of giving written informed consent.
- Female subjects must be post-menopausal or using a highly effective method for avoidance of pregnancy.
- Subjects with a clinical history of COPD in accordance with the following definition by the American Thoracic Society/European Respiratory Society.
- Subject with a measured post-albuterol (salbutamol) FEV1/forced vital capacity(FVC) ratio of <=0.70 at Screening.
- Subjects with a measured post-albuterol (salbutamol) FEV1 <=70% of predicted normal values.
- Subjects with a current or prior history of ≥10 pack-years of cigarette smoking at Screening.

Exclusion Criteria:

- Current diagnosis of asthma. (Subjects with a prior history of asthma are eligible if they have a current diagnosis of COPD).
- Other respiratory disorders (alpha1-antitrypsin deficiency as the underlying cause of COPD, active tuberculosis, lung cancer, bronchiectasis, sarcoidosis, pulmonary fibrosis, pulmonary hypertension, interstitial lung diseases, or other active pulmonary diseases).
- Lung volume reduction surgery within the 12 months prior to Screening.
- Hospitalized due to poorly controlled COPD within 12 weeks of Screening.
- Poorly controlled COPD (occurrence of the following in the 6 weeks prior to Screening -Acute worsening of COPD that is managed by the subject with corticosteroids or antibiotics or that requires treatment prescribed by a physician).
- Lower respiratory tract infection that required the use of antibiotics within 6 weeks prior to Screening.
- Moderate/severe COPD exacerbation/lower respiratory tract infection during Run-In Period.
- Abnormal and clinically significant 12-lead ECG at Screening
- Historical or current evidence of uncontrolled or clinically significant disease like cardiovascular, hypertension, neurological, psychiatric, renal, hepatic, immunological, endocrine (including uncontrolled diabetes or thyroid disease), peptic ulcer disease, or haematological abnormalities. Significant is defined as any disease that, in the opinion of the investigator, would put the safety of the subject at risk through participation, or which would affect the efficacy or safety analysis if the disease/condition exacerbated during the study.
- History of hypersensitivity to any of the study medications or components of the inhalation powder; or history of severe milk protein allergy.
- Known or suspected history of alcohol or drug abuse within the last 2 years.
- Subjects who are medically unable to withhold their albuterol (salbutamol) and/or their ipratropium for the 4-hour period required prior to spirometry testing at each study visit.
- The subject has taken any other investigational drug within 30 days or 5 half-lives of the investigational product (IP) prior to the first dosing day in the current study.
- Use of additional medications prior to Screening (list of medications and time intervals are different for different class of medications and are indicated in the protocol)
- Subjects receiving treatment with long-term oxygen therapy (LTOT) or nocturnal oxygen therapy required for greater than 12 hours a day. Oxygen prn use

(i.e., <=12 hours per day) is not exclusionary.

- Subjects who have participated in the acute phase of a Pulmonary Rehabilitation Program within 4 weeks prior to Screening
- Subjects at risk of non-compliance, or unable to comply with study procedures.
- Study investigators, sub-investigators, study coordinators, employees of a participating investigator or immediate family members of the aforementioned are excluded from participating in this study.
- Women who are pregnant or lactating or are planning on becoming pregnant during the study.
- Previously randomized to either the HZC113109 or HZC112352 clinical studies.

Contacts and Locations

Locations

United States, Florida

GSK Investigational Site

Clearwater, Florida, United States, 33765

GSK Investigational Site

DeLand, Florida, United States, 32720

United States, Idaho

GSK Investigational Site

Coeur D'Alene, Idaho, United States, 83814

United States, Illinois

GSK Investigational Site

Normal, Illinois, United States, 61761

United States, Minnesota

GSK Investigational Site

Woodbury, Minnesota, United States, 55125

United States, North Carolina

GSK Investigational Site

Charlotte, North Carolina, United States, 28207

United States, Ohio

GSK Investigational Site

Columbus, Ohio, United States, 43215

United States, South Carolina

GSK Investigational Site

Easley, South Carolina, United States, 29640

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Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	116974
Health Authority:	United States: Food and Drug Administration

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Study Results

Participant Flow

Recruitment Details

Only those participants that started the Double-blind Treatment Period were considered enrolled.

Pre-Assignment Details

At Visit 1, participants entered a 2-week, single-blind (placebo) Run-in Period to obtain Baseline assessments of salbutamol use and to evaluate adherence with study treatment and procedures, diary card completion, and assessment of disease stability. At Visit 2, participants were randomized to a 12-week, double-blind Treatment Period.

Reporting Groups

	Description
Placebo + Salbutamol	Participants were instructed to take single-blind placebo twice a day (one inhalation from a multi-dose powder inhaler [MPI] and one inhalation from a dry powder inhaler [DPI] in the morning; one inhalation from an MPI in the evening). In addition, all participants received supplemental albuterol (salbutamol) (via a metered dose inhaler [MDI] and/or nebules) to be used on an as-needed basis. Ipratropium bromide alone was permitted, provided that the participant was on a stable dose from Visit 1 (Screening) and remained on the stable dose throughout the study; however, ipratropium must have been withheld for 4 hours prior to and during each clinic visit.
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In

	Description
	addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

2-week Run-in Period

	Placebo + Salbutamol	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Started	993	0	0
Completed	828	0	0
Not Completed	165	0	0
Inclusion/Exclusion Criteria Not Met	140	0	0
Withdrawal by Subject	15	0	0
Physician Decision	4	0	0
Adverse Event	4	0	0
Lost to Follow-up	2	0	0

12-week Double-blind Treatment Period

	Placebo + Salbutamol	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Started	0	412	416
Completed	0	366	371
Not Completed	0	46	45
Adverse Event	0	14	16

	Placebo + Salbutamol	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Lack of Efficacy	0	4	4
Protocol Violation	0	4	2
Protocol-defined Stopping Criteria Met	0	11	9
Lost to Follow-up	0	3	1
Physician Decision	0	2	2
Withdrawal by Subject	0	8	11

Baseline Characteristics

Reporting Groups

	Description
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

Baseline Measures

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID	Total
Number of Participants	412	416	828
Age, Continuous [units: Years] Mean (Standard Deviation)	61.0 (8.17)	61.3 (8.37)	61.1 (8.27)
Gender, Male/Female [units: Participants]			
Female	111	122	233
Male	301	294	595
Race/Ethnicity, Customized [units: participants]			
African American/African Heritage	9	5	14
American Indian or Alaska Native	0	1	1
White-White/Caucasian/European Heritage	403	410	813

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline Trough in Weighted-mean 24-hour Serial Forced Expiratory Volume in One Second (FEV1) on Treatment Day 84
Measure 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 was calculated from the pre-dose FEV1 and the post-dose FEV1 measurements taken at 5, 15, 30, and 60 minutes and 2, 4, 6, 8, 12, 13, 14, 16, 20, and 24 hours on Treatment Day 84. Baseline trough FEV1 was calculated as the mean of the two assessments made 30 minutes pre-dose and 5 minutes pre-dose on Treatment Day 1. The weighted mean was derived by calculating the area under curve, and then dividing by the relevant time interval. The weighted mean change from Baseline was calculated as the weighted mean of the 24-hour serial FEV1 measurements on Day 84 minus the Baseline trough FEV1 value. The analysis used an analysis of covariance (ANCOVA) model with covariates of Baseline FEV1, reversibility stratum, smoking status (at Screening), country, and treatment.
Time Frame	Baseline and Day 84
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all participants who were randomized and received at least one dose of study drug. Only those participants available at the indicated time point were assessed.

Reporting Groups

	Description
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In

	Description
	addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

Measured Values

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Number of Participants Analyzed	350	356
Change From Baseline Trough in Weighted-mean 24-hour Serial Forced Expiratory Volume in One Second (FEV1) on Treatment Day 84 [units: Liters] Least Squares Mean (Standard Error)	0.168 (0.0121)	0.142 (0.0120)

Statistical Analysis 1 for Change From Baseline Trough in Weighted-mean 24-hour Serial Forced Expiratory Volume in One Second (FEV1) on Treatment Day 84

Groups	FF/VI 100/25 µg QD, FP/Salmeterol 250/50 µg BID
Method	ANCOVA
P-Value	0.137
Mean Difference (Net)	0.025
95% Confidence Interval	-0.008 to 0.059

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

2. Secondary Outcome Measure:

Measure Title	Time to Onset on Treatment Day 1
Measure Description	Time to onset on Treatment Day 1 is defined as the time to an increase of 100 milliliters (mL) from Baseline in FEV1 during the 0- to 4-hour serial measurements (5, 15, 30, 60, 120, and 240 minutes post-dose). Participants who never met or exceeded a 100 mL increase over the Baseline value during the 4-hour serial measurements were censored at the actual time of their last FEV1 measurement.
Time Frame	Baseline and Day 1
Safety Issue?	No

Analysis Population Description

ITT Population. Only those participants available at the indicated time point were assessed.

Reporting Groups

	Description
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In

	Description
	addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

Measured Values

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Number of Participants Analyzed	411	416
Time to Onset on Treatment Day 1 [units: Minutes] Median (Full Range)	15 (5 to 240)	15 (5 to 240)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Trough FEV1 on Treatment Day 85
Measure Description	FEV1 is a measure of lung function and is defined as the volume of air that can be forcefully exhaled in one second. Trough FEV1 is defined as the 24-hour FEV1 assessment, which was obtained on Day 85. Baseline trough was calculated as the mean of the two assessments made 30 minutes pre-dose and 5 minutes pre-dose on Treatment Day 1. Change from Baseline was calculated as the average of the Day 85 values minus the Baseline value. The analysis used an analysis of covariance (ANCOVA) model with covariates of Baseline FEV1, reversibility stratum, smoking status (at Screening), country, and treatment.
Time Frame	Baseline and Day 85
Safety Issue?	No

Analysis Population Description

ITT Population. Only those participants available at the indicated time point were assessed.

Reporting Groups

	Description
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

Measured Values

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Number of Participants Analyzed	364	369
Change From Baseline in Trough FEV1 on Treatment Day 85 [units: Liters] Least Squares Mean (Standard Error)	0.151 (0.0126)	0.121 (0.0125)

Reported Adverse Events

Reporting Groups

	Description
FF/VI 100/25 µg QD	Participants received one inhalation of fluticasone furoate/vilanterol (FF/VI) 100/25 micrograms (µg) once daily (QD) in the morning from a DPI and placebo twice daily (BID) from a DPI (one inhalation in the morning and one inhalation in the evening) for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) inhalation to be used as needed throughout the study.
FP/Salmeterol 250/50 µg BID	Participants received fluticasone propionate (FP)/salmeterol 250/50 µg BID from a DPI (one inhalation in the morning and one inhalation in the evening) plus placebo QD in the morning from a DPI for 12 weeks. In addition, participants were provided supplemental albuterol (salbutamol) to be used as needed throughout the study.

Time Frame

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication until Follow-up (up to 12 weeks).

Additional Description

SAEs and non-serious AEs were collected in members of the ITT Population, comprised of all participants who were randomized and received at least one dose of study drug.

Serious Adverse Events

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Total # participants affected/at risk	13/412 (3.16%)	20/416 (4.81%)
Cardiac disorders		
Cardiac failure † [A]		
# participants affected/at	0/412 (0%)	1/416 (0.24%)

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
risk		
# events		
Cardiac failure chronic † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Cardiac failure congestive † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Cor pulmonale † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Coronary artery disease † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Myocardial infarction † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
# events		
Gastrointestinal disorders		
Gastrointestinal haemorrhage † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Hepatobiliary disorders		
Cholecystitis acute † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Infections and infestations		
Cellulitis † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Clostridium difficile colitis † [A]		
# participants affected/at	0/412 (0%)	1/416 (0.24%)

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
risk		
# events		
Infective exacerbation of chronic obstructive airways diseas † [A]		
# participants affected/at risk	0/412 (0%)	3/416 (0.72%)
# events		
Pneumonia † [A]		
# participants affected/at risk	1/412 (0.24%)	4/416 (0.96%)
# events		
Injury, poisoning and procedural complications		
Alcohol poisoning † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Femoral neck fracture † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Fibula fracture † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Mouth injury † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Colon neoplasm † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Small cell lung cancer † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Squamous cell carcinoma of lung † [A]		

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Nervous system disorders		
Cerebral infarction † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Convulsion † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease † [A]		
# participants affected/at risk	5/412 (1.21%)	4/416 (0.96%)
# events		
Haemoptysis † [A]		
# participants affected/at	0/412 (0%)	1/416 (0.24%)

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
risk		
# events		
Pneumothorax † [A]		
# participants affected/at risk	0/412 (0%)	1/416 (0.24%)
# events		
Vascular disorders		
Hypertensive crisis † [A]		
# participants affected/at risk	1/412 (0.24%)	0/416 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 3%

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
Total # participants affected/at risk	46/412 (11.17%)	52/416 (12.5%)
Infections and infestations		
Nasopharyngitis † [A]		

	FF/VI 100/25 µg QD	FP/Salmeterol 250/50 µg BID
# participants affected/at risk	30/412 (7.28%)	26/416 (6.25%)
# events		
Nervous system disorders		
Headache † [A]		
# participants affected/at risk	18/412 (4.37%)	29/416 (6.97%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: GSK Response Center

Organization: GlaxoSmithKline

Phone: 866-435-7343

Email: