Protocol Registration Receipt
05/29/2014

Grantor: CDER IND/IDE Number: 77855 Serial Number:

Randomised Study Comparing the Effects of Inhaled Fluticasone Furoate (FF)/Vilanterol (VI; GW642444M) Combination and FF on an Allergen Induced Asthmatic Response

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	GlaxoSmithKline
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT01128569

Purpose

We propose to use an inhaled allergen challenge model to explore the individual contributions of the components of a novel long-acting beta agonist (LABA)/ inhaled corticosteroid (ICS) combination product on protection from allergic triggers in asthma.

Condition	Intervention	Phase
Asthma	Drug: Fluticasone Furoate	Phase 2

Condition	Intervention	Phase
	Drug: FF/Vilanterol (VI; GW642444M) Drug: Placebo	

Study Type: Interventional
Study Design: Treatment, Crossover Assignment, Double Blind (Subject, Investigator), Randomized, Pharmacodynamics Study
Official Title: A Randomised, Double-blind, Placebo-controlled, Three-way Crossover, Repeat Dose Pilot Study Comparing the Effect of Inhaled Fluticasone Furoate (FF)/Vilanterol (VI; GW642444M) Combination and Fluticasone Furoate on the Allergen-induced Early Asthmatic Response in Subjects With Mild Asthma

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period [Time Frame: Baseline and Day 29 of each treatment period (up to Study Day 197)] [Designated as safety issue: No]

  FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants (par.) were exposed to an allergen (administered by inhalation) 22-23 hours after dosing on Day 28. FEV1 was measured 5 minutes (min), 10 min, 15 min, 20 min, 30 min, and 45 min and 1 hour, 1.5 hours, and 2 hours post-allergen challenge on Day 29. Immediately prior to the exposure of allergen and starting at 2 minutes after inhalation of saline, 3 single measurements of FEV1 were recorded at 1-minute intervals, and the best was taken as the post-saline value. The FEV1 weighted mean was derived by calculating the area under the curve, and then dividing the value by the relevant time interval. Weighted mean change from Baseline is calculated as the weighted mean FEV1 value on Day 29 minus the Baseline value. The Baseline FEV1 value was the post-saline value on Day 29.

Secondary Outcome Measures:

- Maximum Percent Decrease From Baseline in FEV1 Between 0 2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period [Time Frame: Baseline and Day 29 of each treatment period (up to Study Day 197)] [Designated as safety issue: No]

  FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to an allergen 22-23 hours after dosing on Day 28. Immediately prior to the exposure of allergen and starting at 2 minutes (min) after inhalation of saline, 3 single measurements of FEV1were recorded at 1-min intervals, and the best was taken as the post-saline value. The maximum change (i.e., drop in FEV1) from post-saline Baseline (BL) is defined by ordering all of the change from BL values for the 5 min, 10 min, 15 min, 20 min, 30 min, and 45 min and the 1 hour, 1.5 hours, and 2 hours post-allergen challenge and selecting the largest change (i.e., drop in FEV1) from the BL value. If there were no negative change values, indicating a worse FEV1 value as compared to the BL value, the smallest change in FEV1, indicating an improvement from the BL value, was selected. The BL FEV1 value was the post-saline value on Day 29.
- Minimum FEV1 Absolute Change From Baseline Between 0-2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each

Treatment Period [Time Frame: Baseline and Day 29 of each treatment period (up to Study Day 197)] [Designated as safety issue: No]

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to an allergen 22-23 hours after dosing on Day 28. Immediately prior to the exposure of allergen and starting at 2 minutes after inhalation of saline, 3 single measurements of FEV1were recorded at 1-minute intervals, and the best was taken as the post-saline value. The minimum FEV1 over 0-2 hours post-allergen challenge (PAC) (minimum early asthmatic response) was the minimum value of all of the PAC time points up to and including 2 hours PAC (i.e., minimum over 5 minutes (min), 10 min, 15 min, 20 min, 30 min, and 45 min and 1 hour, 1.5 hours, and 2 hours). Change from Baseline was calculated using the post-saline FEV1 on Day 29 as Baseline. Minimum FEV1 absolute change from Baseline between 0-2 hour, following the 22-23 hour post-treatment allergen challenge was calculated as the minimum change value on Day 29 minus the Baseline value

- Number of Participants With Treatment-emergent Adverse Events (AEs) [Time Frame: From the start of study medication until Follow-up/Early Withdrawal (up to 197 days)] [Designated as safety issue: No]

  The number of participants with treatment-emergent AEs was measured. A treatment-emergent adverse event is defined as any event not present prior to the initiation of the treatments, or any event already present that worsens in either intensity of frequency following exposure to the treatments.

Enrollment: 52
Study Start Date: January 2010
Study Completion Date: December 2010
Primary Completion Date: October 2010

Arms	Assigned Interventions
Placebo Comparator: Placebo Placebo Inhaler	Drug: Placebo Placebo Inhaler Other Names: Placebo
Active Comparator: inhaled corticosteroid(ICS)/long acting bronchodilator (LABA) ICS/LABA inhaler	Drug: FF/Vilanterol (VI; GW642444M) FF/VI Other Names: FF/VI
Active Comparator: ICS ICS inhaler	Drug: Fluticasone Furoate FF Other Names: FF

Eligibility

Ages Eligible for Study: 18 Years to 65 Years
Genders Eligible for Study: Both

Inclusion Criteria:

- Body mass index within the range 18.5-35.0 kilograms/metre2 (kg/m2).
- Females of non-child bearing potential.
- Documented history of bronchial asthma, first diagnosed at least 6 months prior to the screening visit and currently being treated only with intermittent short-acting beta -agonist therapy by inhalation
- Pre-bronchodilator FEV1 >70% of predicted at screening
- Subjects who are current non-smokers
- Methacholine challenge PC20 < 8 mg/mL at screening
- Screening allergen challenge demonstrates that the subject experiences an early asthmatic response

Exclusion Criteria:

- Current or chronic history of liver disease, or known hepatic or biliary abnormalities
- Subject is hypertensive at screening
- Respiratory tract infection and/or exacerbation of asthma within 4 weeks prior to the first dose of study medication.
- History of life-threatening asthma
- Symptomatic with hay fever at screening or predicted to have symptomatic hayfever
- Unable to abstain from short acting beta agonists
- Unable to abstain from antihistamines
- Unable to abstain from other medications including non-steroidal anti-inflammatory drugs (NSAIDs), anti-depressant drugs, anti-asthma anti-rhinitis or hay fever medication
- The subject has participated in a study with a new molecular entity during the previous 3 months or has participated in 4 or more clinical studies in the previous 12 months
- undergoing allergen desensitisation therapy

Contacts and Locations

Locations

Germany

GSK Investigational Site

Berlin, Berlin, Germany, 14050

New Zealand

GSK Investigational Site

Wellington, New Zealand, 6021

United Kingdom

GSK Investigational Site

London, United Kingdom, NW10 7EW

GSK Investigational Site

Manchester, United Kingdom, M23 9QZ

Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Publications:

Oliver A, Ayer J, Quinn D, Goldfrad C, van Hecke B, Boyce M . Does combined fluticasone furoate / vilanterol reduce the fall in lung function following inhaled allergen 23h after dosing in adult asthma? A randomised, controlled trial. [Clin Transl Allergy]. 2012;2:11.

Responsible Party:	GlaxoSmithKline
Study ID Numbers:	113090
Health Authority:	United Kingdom: Medicines and Healthcare Products Regulatory Agency Germany: Bundesinstitut für Arzneimittel und Medizinprodukte New Zealand: Wellington Ethics Committee New Zealand: Medicines and Medical Devices Safety Authority Germany: Berlin Ethics Committee United Kingdom: NRES Head Office, National Patient Safety Agency United States: Food and Drug Administration

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Study Results

Participant Flow

Recruitment Details

Participants were screened within 42 days of the first dose, conducted over 2 days (not consecutive days). During this time, a methacholine challenge and an allergen challenge test were performed. Participants meeting all inclusion criteria and none of the exclusion criteria were randomized to 3 study treatment periods, each lasting 28 days.

Pre-Assignment Details

This study was a multi-center, randomized, double-blind, placebo controlled, three-period crossover study in mild asthmatic male and female participants. Following the Run-in period, participants were randomized to 1 of 6 treatment sequences of placebo, FF 100 micrograms (µg) once daily (OD), and FF/VI 100/25 µg OD.

Reporting Groups

	Description
Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Participants received placebo, Fluticasone Furoate (FF) 100 micrograms (µg), and FF/Vilanterol (VI) 100/25 µg in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day (OD) in the evening from a Dry Powder Inhaler (DPI) for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Participants received placebo, FF/VI 100/25 µg, and FF 100 µg in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day in the evening from a DPI for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Participants received FF 100 µg, FF/VI 100/25 µg, and placebo in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day in the evening from a DPI for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.

	Description
Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Participants received FF 100 µg, placebo, and FF/VI 100/25 µg in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day in the evening from a DPI for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Participants received FF/VI 100/25 µg, placebo, and FF 100 µg in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day in the evening from a DPI for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo	Participants received FF/VI 100/25 µg, FF 100 µg, and placebo in Treatment Periods 1, 2, and 3, respectively. Participants received all treatments once a day in the evening from a DPI for 28 days. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.

Treatment Period 1

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Started	9	8	9	8	9	9
Completed	9	8	9	8	9	9
Not Completed	0	0	0	0	0	0

Washout Period 1

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Started	9	8	9	8	9	9
Completed	9	8	8	8	9	9
Not Completed	0	0	1	0	0	0
Adverse Event	0	0	1	0	0	0

Treatment Period 2

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Started	9	8	8	8	9	9
Completed	9	7	8	8	9	9
Not Completed	0	1	0	0	0	0
Withdrawal by Subject	0	1	0	0	0	0

Washout Period 2

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Started	9	7	8	8	9	9

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Completed	9	7	8	8	9	9
Not Completed	0	0	0	0	0	0

Treatment Period 3

	Sequence 1: Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: Placebo, FF/VI 100/25 µg, FF 100 µg	Sequence 3: FF 100 µg, FF/VI 100/25 µg, Placebo	Sequence 4: FF 100 µg, Placebo, FF/VI 100/25 µg	Sequence 5: FF/VI 100/25 µg, Placebo, FF 100 µg	Sequence 6: FF/VI 100/25 µg, FF 100 µg, Placebo
Started	9	7	8	8	9	9
Completed	9	7	8	8	9	9
Not Completed	0	0	0	0	0	0

Baseline Characteristics

Reporting Groups

	Description
Placebo, FF 100 µg OD, FF/VI 100/25 µg OD in 1 of 6 Sequences	All participants received one of the following three treatments in one of three treatment periods once daily (OD) in the evening from the Dry Powder Inhaler (DPI) for 28 days: Placebo, Fluticasone Furoate (FF) 100 microgram (µg) dry inhalation powder, and FF/Vilanterol (FF/VI) 100/25 µg dry inhalation powder. Participants were randomized to receive treatment in one of the six following sequences: (1) Placebo, FF 100 µg, FF/VI 100/25 µg; (2) Placebo, FF/VI 100/25 µg, FF 100 µg; (3) FF 100 µg, FF/VI 100/25 µg, Placebo; (4) FF 100 µg, Placebo,

	Description
	FF/VI 100/25 µg; (5) FF/VI 100/25 µg, Placebo, FF 100 µg; (6) FF/VI 100/25 µg, FF 100 µg, Placebo. The three treatment periods were separated by a washout period of at least 21 days (from the Day 28 dose) and a maximum of 35 days.

Baseline Measures

	Placebo, FF 100 µg OD, FF/VI 100/25 µg OD in 1 of 6 Sequences
Number of Participants	52
Age, Continuous [units: Years] Mean (Standard Deviation)	35.4 (8.63)
Gender, Male/Female [units: Participants]	
Female	18
Male	34
Race/Ethnicity, Customized [units: participants]	
White - White/Caucasian/European Heritage	48
African American/African Heritage	2
Asian - South East Asian Heritage	1

	Placebo, FF 100 µg OD, FF/VI 100/25 µg OD in 1 of 6 Sequences
Mixed Race	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period
Measure Description	FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants (par.) were exposed to an allergen (administered by inhalation) 22-23 hours after dosing on Day 28. FEV1 was measured 5 minutes (min), 10 min, 15 min, 20 min, 30 min, and 45 min and 1 hour, 1.5 hours, and 2 hours post-allergen challenge on Day 29. Immediately prior to the exposure of allergen and starting at 2 minutes after inhalation of saline, 3 single measurements of FEV1 were recorded at 1-minute intervals, and the best was taken as the post-saline value. The FEV1 weighted mean was derived by calculating the area under the curve, and then dividing the value by the relevant time interval. Weighted mean change from Baseline is calculated as the weighted mean FEV1 value on Day 29 minus the Baseline value. The Baseline FEV1 value was the post-saline value on Day 29.
Time Frame	Baseline and Day 29 of each treatment period (up to Study Day 197)

Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: par. randomized to treatment who received >=1 dose of study drug. Only those par. available at the specified time points were analyzed. Analysis was performed using mixed model analysis of covariance (ANCOVA) with fixed effects of treatment, period, par.-level Baseline, period level Baseline, country, sex, and age.

Reporting Groups

	Description
Placebo	Participants received Placebo OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
FF 100 µg OD	Participants received FF 100 µg dry inhalation powder OD in the evening from the DPI for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg dry inhalation powder OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.

Measured Values

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Number of Participants Analyzed	45	49	46
Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen	-0.372 (0.0557)	-0.210 (0.0549)	-0.227 (0.0550)

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Challenge on Day 29 of Each Treatment Period [units: Liters] Least Squares Mean (Standard Error)			

Statistical Analysis 1 for Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period

Groups	Placebo, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.162
95% Confidence Interval	0.087 to 0.237

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

[Not specified.]

Statistical Analysis 2 for Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period

Groups	Placebo, FF/VI 100/25 µg OD
Method	
Mean Difference (Final Values)	0.145
95% Confidence Interval	0.069 to 0.222

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

[Not specified.]

Statistical Analysis 3 for Weighted Mean Change From Baseline in Forced Expiratory Volume in One Second (FEV1) Between 0-2 Hours, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period

Groups	FF 100 µg OD, FF/VI 100/25 µg OD

Method	
Mean Difference (Final Values)	-0.017
95% Confidence Interval	-0.091 to 0.057

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

[Not specified.]

2. Secondary Outcome Measure:

Measure Title	Maximum Percent Decrease From Baseline in FEV1 Between 0 2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period
Measure Description	FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to an allergen 22-23 hours after dosing on Day 28. Immediately prior to the exposure of allergen and starting at 2 minutes (min) after inhalation of saline, 3 single measurements of FEV1were recorded at 1-min intervals, and the best was taken as the post-saline value. The maximum change (i.e., drop in FEV1) from post-saline Baseline (BL) is defined by ordering all of the change from BL values for the 5 min, 10 min, 15 min, 20 min, 30 min, and 45 min and the 1 hour, 1.5 hours, and 2 hours post-allergen challenge and selecting the largest change (i.e., drop in FEV1) from the BL value. If there were no negative change values, indicating a worse FEV1 value as compared to the BL value, the smallest change in FEV1, indicating an improvement from the BL value, was selected. The BL FEV1 value was the post-saline value on Day 29.
Time Frame	Baseline and Day 29 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

ITT Population. Only those participants available at the specified time points were analyzed. Analysis was performed using mixed model analysis of covariance (ANCOVA) with fixed effects of treatment, period, participant-level BL, period level BL, country, sex, and age. Change from BL was calculated as the value on Day 29 minus the BL value.

Reporting Groups

	Description
Placebo	Participants received Placebo OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
FF 100 µg OD	Participants received FF 100 µg dry inhalation powder OD in the evening from the DPI for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg dry inhalation powder OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.

Measured Values

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Number of Participants Analyzed	45	49	46
Maximum Percent Decrease From Baseline in FEV1 Between 0 2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period [units: Percent change] Least Squares Mean (Standard Error)	-24.991 (2.0736)	-14.040 (2.0435)	-13.206 (2.0491)

3. Secondary Outcome Measure:

Measure Title	Minimum FEV1 Absolute Change From Baseline Between 0-2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period
Measure Description	FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Participants were exposed to an allergen 22-23 hours after dosing on Day 28. Immediately prior to the exposure of allergen and starting at 2 minutes after inhalation of saline, 3 single measurements of FEV1were recorded at 1-minute intervals, and the best was taken as the post-saline value. The minimum FEV1 over 0-2 hours post-allergen challenge (PAC) (minimum early asthmatic response) was the minimum value of all of the PAC time points up to and including 2 hours PAC (i.e., minimum over 5 minutes (min), 10 min, 15 min, 20 min, 30 min, and 45 min and 1 hour, 1.5 hours, and 2 hours). Change from Baseline was calculated using the post-saline FEV1 on Day 29 as Baseline. Minimum FEV1 absolute change from Baseline between 0–2 hour, following the 22–23 hour post-treatment allergen challenge was calculated as the minimum change value on Day 29 minus the Baseline value
Time Frame	Baseline and Day 29 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

ITT Population. Only those participants available at the specified time points were analyzed. Analysis was performed using mixed model ANCOVA with fixed effects of treatment, period, participant-level Baseline, period level Baseline, country, sex, and age.

Reporting Groups

	Description
Placebo	Participants received Placebo OD from the DPI in the evening for 28

	Description
	days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
FF 100 µg OD	Participants received FF 100 µg dry inhalation powder OD in the evening from the DPI for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg dry inhalation powder OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.

Measured Values

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Number of Participants Analyzed	45	49	46
Minimum FEV1 Absolute Change From Baseline Between 0-2 Hour, Following the 22-23 Hour Post-treatment Allergen Challenge on Day 29 of Each Treatment Period [units: Liters] Least Squares Mean (Standard Error)	-0.809 (0.0775)	-0.479 (0.0765)	-0.478 (0.0767)

4. Secondary Outcome Measure:

Measure Title	Number of Participants With Treatment-emergent Adverse Events (AEs)

Measure Description	The number of participants with treatment-emergent AEs was measured. A treatment-emergent adverse event is defined as any event not present prior to the initiation of the treatments, or any event already present that worsens in either intensity of frequency following exposure to the treatments.
Time Frame	From the start of study medication until Follow-up/Early Withdrawal (up to 197 days)
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Placebo	Participants received Placebo OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
FF 100 µg OD	Participants received FF 100 µg dry inhalation powder OD in the evening from the DPI for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg dry inhalation powder OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.

Measured Values

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Number of Participants Analyzed	51	51	51
Number of Participants With Treatment-emergent Adverse Events (AEs) [units: participants]	20	22	18

Reported Adverse Events

Reporting Groups

	Description
Placebo	Participants received Placebo OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from the Day 28 dose) and a maximum of 35 days.
FF 100 µg OD	Participants received FF 100 µg dry inhalation powder OD in the evening from the DPI for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg dry inhalation powder OD from the DPI in the evening for 28 days during one of the three treatment periods. Each treatment period was followed by a washout of at least 21 days (from Day 28 dose) and a maximum of 35 days.

Time Frame

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication until Follow-up/Early Withdrawal (up to 197 days).

Additional Description

SAEs and non-serious AEs were reported for members of the Intent-to-Treat (ITT) Population, comprised of all participants randomized to treatment who received at least one dose of study drug.

Serious Adverse Events

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Total # participants affected/at risk	0/51 (0%)	0/51 (0%)	0/51 (0%)

Other Adverse Events

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

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Total # participants affected/at risk	15/51 (29.41%)	18/51 (35.29%)	11/51 (21.57%)
Gastrointestinal disorders			
Mouth ulceration †[A]			
# participants affected/at risk	0/51 (0%)	2/51 (3.92%)	2/51 (3.92%)
# events			
Nausea †[A]			
# participants affected/at risk	2/51 (3.92%)	2/51 (3.92%)	0/51 (0%)
# events			
General disorders			

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
Chest discomfort †[A]			
# participants affected/at risk	3/51 (5.88%)	0/51 (0%)	0/51 (0%)
# events			
Infections and infestations			
Nasopharyngitis †[A]			
# participants affected/at risk	3/51 (5.88%)	2/51 (3.92%)	0/51 (0%)
# events			
Nervous system disorders			
Headache †[A]			
# participants affected/at risk	9/51 (17.65%)	11/51 (21.57%)	5/51 (9.8%)
# events			
Respiratory, thoracic and mediastinal disorders			
Cough †[A]			
# participants affected/at risk	1/51 (1.96%)	3/51 (5.88%)	0/51 (0%)
# events			
Dysphonia †[A]			

	Placebo	FF 100 µg OD	FF/VI 100/25 µg OD
# participants affected/at risk	0/51 (0%)	2/51 (3.92%)	2/51 (3.92%)
# events			
Oropharyngeal pain †[A]			
# participants affected/at risk	2/51 (3.92%)	2/51 (3.92%)	2/51 (3.92%)
# 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: