Protocol Registration Receipt
08/22/2013

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

Randomised Study Comparing the Effects of Inhaled FF/GW642444M Combination, FF and GW642444M on an Allergen Induced Asthmatic Response

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	GlaxoSmithKline
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT01128595

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/ inhaled corticosteroid combination product and its components on protection from allergic triggers in asthma

Condition	Intervention	Phase
Asthma	Drug: FF/GW642444M	Phase 2

Condition	Intervention	Phase
	Drug: GW642444M Drug: Fluticasone Furoate 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, Four-way Crossover, Repeat Dose Study Comparing the Effect of Inhaled Fluticasone Furoate/GW642444M Combination, GW642444M and Fluticasone Furoate on the Allergen-induced Asthmatic Response in Subjects With Mild Asthma

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [Time Frame: Day 21 of each treatment period (up to Study Day 197)] [Designated as safety issue: No]

  Forced expiratory volume in one second (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 (administered by inhalation) 1 hr after dosing on Day 21. Minimum FEV1 over 4-10 hours post-allergen challenge (minimum LAR) is the minimum value of all of the post-saline time points between 4 and 10 hrs post-allergen challenge, inclusive of the 4 hr and 10 hr timepoints (i.e., minimum over 4 hrs, 4.5 hrs, 5 hrs, 5.5 hrs, 6 hrs, 6.5 hrs, 7 hrs, 7.5 hrs, 8 hrs, 8.5 hrs, 9 hrs, 9.5 hrs, and 10 hrs). Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.

- LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [Time Frame: Day 21 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 1 hour after dosing on Day 21. LAR FEV1 was measured 4 hrs, 4.5 hrs, 5 hrs, 5.5 hrs, 6 hrs, 6.5 hrs, 7 hrs, 7.5 hrs, 8 hrs, 8.5 hrs, 9 hrs, 9.5 hrs, and 10 hrs post-allergen challenge on Day 21. Absolute change from saline in WM FEV1 was calculated as the area under the curve divided by the relevant time interval and subtracting the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.

- Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [Time Frame: Day 21 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 1 hr after dosing on Day 21. Minimum FEV1 over 0-2 hrs post-allergen challenge (Minimum EAR) is the minimum value of all of the post-allergen challenge timepoints up to and including 2 hours post-allergen challenge (i.e., minimum over 5 minutes (min), 10 min, 15 min, 20 min, 30 min, 45 min and 1 hr, 1.5 hrs, and 2 hrs. Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1

value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.

- EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [Time Frame: Day 21 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 1 hr after dosing on Day 21. The EAR FEV1 was measured 0 minutes (min), 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 1 hr, 1.5 hrs, and 2 hrs post-allergen challenge on Day 21. Least squares means were obtained by adjusting for period and participant and period Baselines. Absolute change from saline in WM FEV1 was calculated as the area under the curve divided by the relevant time interval and subtracting the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value.

Secondary Outcome Measures:

- Maximum Percent Change From Saline in FEV1 Between 0-2 Hrs, Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [Time Frame: Day 21 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 1 hr after dosing on Day 21. FEV1 was measured 0 minutes (min), 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 1 hr, 1.5 hrs, and 2 hrs post-allergen challenge on Day 21. Maximum percent change was calculated as the minimum FEV1 minus the saline FEV1 value divided by the saline FEV1 multiplied by 100. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline FEV1 value.

- Provocative Concentration of Methacholine Estimated to Result in a 20% Reduction in FEV1 (PC20) on Day 22 of Each Treatment Period [Time Frame: Day 22 of each treatment period (up to Study Day 198)] [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 inhaled doubling increments of methacholine until a >=20% fall in FEV1 from the saline value was achieved. After inhalation of saline, 3 measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value.

Enrollment: 27
Study Start Date: May 2010
Study Completion Date: August 2011
Primary Completion Date: August 2011

Arms	Assigned Interventions
Active Comparator: ICS	Drug: Fluticasone Furoate
Active Comparator: ICS/LABA	Drug: FF/GW642444M
Active Comparator: LABA	Drug: GW642444M

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo

Asthma is an increasingly common disease and is essentially caused by an allergic type of reaction of the immune system. Airways of the lungs become inflamed and narrow as a result of a reaction to triggers like chemicals (house-hold cleaning products, pollution) and allergens (house dust mite and cat or dog fur). The airways become blocked, causing shortness of breath and wheezing. The purpose of this study is to find out more information about how effective the study drugs are at protecting the lungs against allergic triggers of asthma. There are three study drugs being investigated in this study: fluticasone furoate on its own, GW642444M on its own and a combination of fluticasone furoate (FF) and GW642444M.

FF is a corticosteroid that is being developed by for the treatment of asthma. A nasal spray formulation of FF has been approved for marketing in the USA, Europe and Japan for the treatment of hayfever (rhinitis) but the dry powder formulation used in this study is not yet approved.

GW642444M is a long-acting beta2-agonist being developed by GSK for the treatment of chronic obstructive pulmonary disease (COPD). It works by acting on cells in the lungs, causing some of the muscles around the lungs to relax and open up better (bronchodilation), making breathing easier. The combination of FF/GW642444M is being developed as a once-daily treatment for both asthma and COPD.

Study treatment will be taken for 21 days in each period (4 treatment periods: FF alone, GW642444M alone, FF/GW64244M combination and placebo) and each subject will receive all treatments. On D21 subjects will undergo an allergen challenge, followed by a methacholine challenge on D22. The washout between treatment periods will be 21-35 days.

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

Australia, New South Wales

GSK Investigational Site

Randwick, New South Wales, Australia, 2031

New Zealand

GSK Investigational Site

Wellington, New Zealand, 6021

Sweden

GSK Investigational Site

Göteborg, Sweden, SE-413 45

GSK Investigational Site

Lund, Sweden, SE-221 85

Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party: GlaxoSmithKline
Study ID Numbers: 113126
Health Authority: New Zealand: Medsafe
United States: Food and Drug Administration
Sweden: Medical Products Agency
Australia: Therapeutic Goods Administration

Study Results

Participant Flow

Pre-Assignment Details

Participants meeting all of the inclusion criteria and none of the exclusion criteria during the Screening Visit, conducted 14-42 days prior to the first dose of study medication, entered a 14-day Run-in Period. Participants were then randomized to 4 Treatment Periods, each lasting 21 days and separated by a nominal washout period of 21-35 days.

Reporting Groups

	Description
Sequence 1: VI 25 µg, Placebo, FF 100 µg, FF/VI 100/25 µg	Participants received Vilanterol (VI) 25 micrograms (µg), placebo, fluticasone furoate (FF) 100 µg, and FF/VI 100/25 µg in Treatment Periods 1, 2, 3, and 4, respectively. Participants received all treatments once a day (OD) for 21 days from a Dry Powder Inhaler (DPI). The four treatment periods were separated by a washout period of 21 to 35 days.
Sequence 2: FF/VI 100/25 µg, FF 100 µg, Placebo, VI 25 µg	Participants received FF/VI 100/25 µg, FF 100 µg, placebo, and VI 25 µg in Treatment Periods 1, 2, 3, and 4, respectively. Participants received all treatments once a day (OD) for 21 days from a Dry Powder Inhaler (DPI). The four treatment periods were separated by a washout

	Description
	period of 21 to 35 days.
Sequence 3: Placebo, FF/VI 100/25 µg, VI 25 µg, FF 100 µg	Participants received placebo, FF/VI 100/25 µg, VI 25 µg, and FF 100 µg in Treatment Periods 1, 2, 3, and 4, respectively. Participants received all treatments once a day (OD) for 21 days from a Dry Powder Inhaler (DPI). The four treatment periods were separated by a washout period of 21 to 35 days.
Sequence 4: FF 100 µg, VI 25 µg, FF/VI 100/25 µg, Placebo	Participants received FF 100 µg, VI 25 µg, FF/VI 100/25 µg, and placebo in Treatment Periods 1, 2, 3, and 4, respectively. Participants received all treatments once a day (OD) for 21 days from a Dry Powder Inhaler (DPI). The four treatment periods were separated by a washout period of 21 to 35 days.

Treatment Period 1

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

Washout Period 1

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

Treatment Period 2

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

Washout Period 2

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

Treatment Period 3

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

Washout Period 3

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

Treatment Period 4

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

	Sequence 1: VI 25 µg, Placebo, FF 100 µg, FF/VI 100/25 µg	Sequence 2: FF/VI 100/25 µg, FF 100 µg, Placebo, VI 25 µg	Sequence 3: Placebo, FF/VI 100/25 µg, VI 25 µg, FF 100 µg	Sequence 4: FF 100 µg, VI 25 µg, FF/VI 100/25 µg, Placebo
Not Completed	0	0	0	0

Baseline Characteristics

Reporting Groups

	Description
Placebo, FF/VI 100/25 µg OD, FF 100 µg OD, VI 25 µg	All participants received one of the following four treatments in one of four treatment periods once daily (OD) from the Dry Powder Inhaler (DPI) for 21 days: Placebo; Fluticasone Furoate /Vilanterol (FF/VI) 100/25 microgram (µg) dry inhalation powder; Fluticasone Furoate (FF) 100 µg dry inhalation powder; and Vilanterol (VI) 25 µg dry inhalation powder. Participants were randomized to receive treatment in one of the four following sequences: (1) VI 25 µg, Placebo, FF 100 µg, FF/VI 100/25 µg; (2) FF/VI 100/25 µg, FF 100 µg, Placebo, VI 25 µg; (3) Placebo, FF/VI 100/25 µg, VI 25 µg, FF 100 µg; (4) FF 100 µg, VI 25 µg, FF/VI 100/25 µg, Placebo. The four treatment periods were separated by a washout period of 21 to 35 days.

Baseline Measures

	Placebo, FF/VI 100/25 µg OD, FF 100 µg OD, VI 25 µg
Number of Participants	27

	Placebo, FF/VI 100/25 µg OD, FF 100 µg OD, VI 25 µg
Age, Continuous [units: Years] Mean (Standard Deviation)	30.8 (7.46)
Gender, Male/Female [units: Participants]	
Female	8
Male	19
Race/Ethnicity, Customized [units: participants]	
White/Caucasian/European Heritage	25
East Asian Heritage	1
Mixed Race	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period
Measure Description	Forced expiratory volume in one second (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 (administered by inhalation) 1 hr after dosing on Day 21. Minimum FEV1 over 4-10 hours post-allergen challenge (minimum LAR) is the minimum value of all of the post-saline time points between 4 and 10 hrs post-allergen challenge, inclusive of the 4 hr and 10 hr timepoints (i.e., minimum over 4 hrs, 4.5 hrs, 5 hrs, 5.5 hrs, 6 hrs, 6.5 hrs, 7 hrs, 7.5 hrs, 8 hrs, 8.5 hrs, 9 hrs, 9.5 hrs, and 10 hrs). Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.
Time Frame	Day 21 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

Efficacy Population: all participants who received at least one dose of study medication, had a post-dose FEV1 assessment, and who were not major protocol violators. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a

	Description
	washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	20	26	27	22
Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [units: Liters] Least Squares Mean (95% Confidence Interval)	-0.731 (-0.878 to -0.584)	-0.216 (-0.343 to -0.088)	-0.188 (-0.315 to -0.061)	-0.536 (-0.676 to -0.396)

Statistical Analysis 1 for Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF/VI 100/25 µg OD
Method	
Mean Difference (Final Values)	0.515
95% Confidence Interval	0.330 to 0.701

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

[Not specified.]

Statistical Analysis 2 for Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF 100 µg OD
Method	

Mean Difference (Final Values)	0.543
95% Confidence Interval	0.355 to 0.730

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

[Not specified.]

Statistical Analysis 3 for Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.195
95% Confidence Interval	0.001 to 0.388

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

[Not specified.]

Statistical Analysis 4 for Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, FF 100 µg OD
Method	
Mean Difference (Final Values)	-0.027
95% Confidence Interval	-0.198 to 0.143

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

[Not specified.]

Statistical Analysis 5 for Late Asthmatic Response (LAR): Absolute Change From Saline in Minimum FEV1 Between 4-10 Hours (Hrs) Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

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

Mean Difference (Final Values)	0.320
95% Confidence Interval	0.140 to 0.501

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

[Not specified.]

2. Primary Outcome Measure:

Measure Title	LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 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 1 hour after dosing on Day 21. LAR FEV1 was measured 4 hrs, 4.5 hrs, 5 hrs, 5.5 hrs, 6 hrs, 6.5 hrs, 7 hrs, 7.5 hrs, 8 hrs, 8.5 hrs, 9 hrs, 9.5 hrs, and 10 hrs post-allergen challenge on Day 21. Absolute change from saline in WM FEV1 was calculated as the area under the curve divided by the relevant time interval and subtracting the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.
Time Frame	Day 21 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

Efficacy Population. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	20	26	27	22
LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [units: Liters] Least Squares Mean (95% Confidence Interval)	-0.466 (-0.589 to -0.343)	0.018 (-0.089 to 0.125)	0.018 (-0.089 to 0.124)	-0.298 (-0.415 to -0.181)

Statistical Analysis 1 for LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF/VI 100/25 µg OD

Method	
Mean Difference (Final Values)	0.484
95% Confidence Interval	0.332 to 0.636

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

[Not specified.]

Statistical Analysis 2 for LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.484
95% Confidence Interval	0.330 to 0.638

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

[Not specified.]

Statistical Analysis 3 for LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.168
95% Confidence Interval	0.009 to 0.327

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

[Not specified.]

Statistical Analysis 4 for LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

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

Method	
Mean Difference (Final Values)	0.000
95% Confidence Interval	-0.140 to 0.140

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

[Not specified.]

Statistical Analysis 5 for LAR: Absolute Change From Saline in Weighted Mean (WM) FEV1 Between 4-10 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.316
95% Confidence Interval	0.168 to 0.464

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

[Not specified.]

3. Primary Outcome Measure:

Measure Title	Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 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 1 hr after dosing on Day 21. Minimum FEV1 over 0-2 hrs post-allergen challenge (Minimum EAR) is the minimum value of all of the post-allergen challenge timepoints up to and including 2 hours post-allergen challenge (i.e., minimum over 5 minutes (min), 10 min, 15 min, 20 min, 30 min, 45 min and 1 hr, 1.5

	hrs, and 2 hrs. Absolute change from saline in minimum FEV1 was calculated as the minimum FEV1 minus the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value. Least squares means were obtained by adjusting for period and participant and period Baselines.
Time Frame	Day 21 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

Efficacy Population. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	22	27	27	22
Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [units: Liters] Least Squares Mean (95% Confidence Interval)	-1.091 (-1.344 to -0.837)	-0.614 (-0.858 to -0.370)	-0.826 (-1.070 to -0.581)	-0.955 (-1.209 to -0.702)

Statistical Analysis 1 for Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.212
95% Confidence Interval	0.031 to 0.393

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

[Not specified.]

Statistical Analysis 2 for Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.341
95% Confidence Interval	0.147 to 0.536

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

[Not specified.]

Statistical Analysis 3 for Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF/VI 100/25 µg OD
Method	
Mean Difference (Final Values)	0.477
95% Confidence Interval	0.282 to 0.672

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

[Not specified.]

Statistical Analysis 4 for Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.265
95% Confidence Interval	0.066 to 0.463

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

[Not specified.]

Statistical Analysis 5 for Early Asthmatic Response (EAR): Absolute Change From Saline in Minimum FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.135
95% Confidence Interval	-0.072 to 0.343

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

[Not specified.]

4. Primary Outcome Measure:

Measure Title	EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 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 1 hr after dosing on Day 21. The EAR FEV1 was measured 0 minutes (min), 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 1 hr, 1.5 hrs, and 2 hrs post-allergen challenge on Day 21. Least squares means were obtained by adjusting for period and participant and period Baselines. Absolute change from saline in WM FEV1 was calculated as the area under the curve divided by the relevant time interval and subtracting the saline FEV1 value. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value.
Time Frame	Day 21 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

Efficacy Population. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days

	Description
	during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	22	27	27	22
EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [units: Liters] Least Squares Mean (95% Confidence Interval)	-0.560 (-0.745 to -0.374)	-0.297 (-0.476 to -0.118)	-0.386 (-0.565 to -0.207)	-0.533 (-0.718 to -0.348)

Statistical Analysis 1 for EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.089
95% Confidence Interval	-0.037 to 0.215

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

[Not specified.]

Statistical Analysis 2 for EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	FF/VI 100/25 µg OD, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.236
95% Confidence Interval	0.101 to 0.371

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

[Not specified.]

Statistical Analysis 3 for EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF/VI 100/25 µg OD
Method	
Mean Difference (Final Values)	0.263
95% Confidence Interval	0.127 to 0.398

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

[Not specified.]

Statistical Analysis 4 for EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, FF 100 µg OD
Method	
Mean Difference (Final Values)	0.174
95% Confidence Interval	0.036 to 0.312

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

[Not specified.]

Statistical Analysis 5 for EAR: Absolute Change From Saline in Weighted Mean FEV1 Between 0-2 Hrs Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period

Groups	Placebo, VI 25 µg OD
Method	
Mean Difference (Final Values)	0.026
95% Confidence Interval	-0.118 to 0.171

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

[Not specified.]

5. Secondary Outcome Measure:

Measure Title	Maximum Percent Change From Saline in FEV1 Between 0-2 Hrs, Following the 1-hr Post-treatment Allergen Challenge on Day 21 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 1 hr after dosing on Day 21. FEV1 was measured 0 minutes (min), 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 1 hr, 1.5 hrs, and 2 hrs post-allergen challenge on Day 21. Maximum percent change was calculated as the minimum FEV1 minus the saline FEV1 value divided by the saline FEV1 multiplied by 100. After inhalation of saline, 3 single measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline FEV1 value.
Time Frame	Day 21 of each treatment period (up to Study Day 197)
Safety Issue?	No

Analysis Population Description

Efficacy Population. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	22	27	27	22
Maximum Percent Change From Saline in FEV1 Between 0-2 Hrs, Following the 1-hr Post-treatment Allergen Challenge on Day 21 of Each Treatment Period [units: percent change] Median (Full Range)	-26.13 (-58.9 to -5.4)	-10.43 (-58.9 to -2.1)	-16.14 (-64.9 to -4.0)	-18.35 (-59.3 to -4.4)

6. Secondary Outcome Measure:

Measure Title	Provocative Concentration of Methacholine Estimated to Result in a 20% Reduction in FEV1 (PC20) on Day 22 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 inhaled doubling increments of methacholine until a >=20% fall in FEV1 from the saline value was achieved. After inhalation of saline, 3 measurements of FEV1 were recorded; the maximum FEV1 value was taken as the saline value.
Time Frame	Day 22 of each treatment period (up to Study Day 198)
Safety Issue?	No

Analysis Population Description

Efficacy Population. Only those participants available at the specified time points were analyzed.

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

	Description
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Measured Values

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Number of Participants Analyzed	23	27	25	24
Provocative Concentration of Methacholine Estimated to Result in a 20% Reduction in FEV1 (PC20) on Day 22 of Each Treatment Period [units: milligrams per milliliter] Mean (Standard Deviation)	1.046 (3.3191)	2.500 (3.7363)	2.492 (5.3371)	0.387 (0.5311)

Reported Adverse Events

Reporting Groups

	Description
Placebo	Participants received placebo OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF/VI 100/25 µg OD	Participants received FF/VI 100/25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.
FF 100 µg OD	Participants received FF 100 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed

	Description
	by a washout period of 21-35 days.
VI 25 µg OD	Participants received VI 25 µg OD from the DPI for 21 days during one of the four treatment periods. Each treatment period was followed by a washout period of 21-35 days.

Time Frame

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication to the end of the fourth treatment period (up to Day 210).

Additional Description

SAEs and non-serious AEs were reported for members of the All Participants Population, comprised of all participants who received at least one dose of study medication.

Serious Adverse Events

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Total # participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	0/26 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Total # participants affected/at risk	19/27 (70.37%)	20/27 (74.07%)	19/27 (70.37%)	22/26 (84.62%)
Ear and labyrinth disorders				
Ear pain † [A]				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Eye disorders				
Conjunctivitis † [A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	1/27 (3.7%)	0/26 (0%)
# events				
Gastrointestinal disorders				
Abdominal discomfort † [A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Abdominal pain upper † [A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Dental caries † [A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Diarrhoea † [A]				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	2/26 (7.69%)
# events				
Dyspepsia †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	1/27 (3.7%)	1/26 (3.85%)
# events				
Dysphagia †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Gastritis †[A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Gastrooesophageal reflux disease †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Nausea †[A]				
# participants affected/at risk	1/27 (3.7%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# events				
Toothache †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	1/26 (3.85%)
# events				
Vomiting †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	1/27 (3.7%)	1/26 (3.85%)
# events				
Immune system disorders				
Seasonal allergy †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	3/27 (11.11%)	1/26 (3.85%)
# events				
Infections and infestations				
Eczema infected †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Gastroenteritis †[A]				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# participants affected/at risk	0/27 (0%)	0/27 (0%)	1/27 (3.7%)	0/26 (0%)
# events				
Nasopharyngitis †[A]				
# participants affected/at risk	2/27 (7.41%)	3/27 (11.11%)	2/27 (7.41%)	5/26 (19.23%)
# events				
Oral candidiasis †[A]				
# participants affected/at risk	2/27 (7.41%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Oral herpes †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Pharyngitis †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Rhinitis †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	1/27 (3.7%)	0/26 (0%)
# events				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Sinusitis †[A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Tinea infection †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Tooth infection †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Upper respiratory tract infection †[A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Viral upper respiratory tract infection †[A]				
# participants affected/at risk	1/27 (3.7%)	2/27 (7.41%)	0/27 (0%)	0/26 (0%)
# events				
Injury, poisoning and				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
procedural complications				
Eye penetration † [A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Foot fracture † [A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Joint injury † [A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Joint sprain † [A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Muscle strain † [A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	1/26 (3.85%)
# events				
Procedural pain † [A]				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Tooth fracture † [A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Musculoskeletal and connective tissue disorders				
Arthralgia † [A]				
# participants affected/at risk	0/27 (0%)	2/27 (7.41%)	1/27 (3.7%)	0/26 (0%)
# events				
Back pain † [A]				
# participants affected/at risk	1/27 (3.7%)	1/27 (3.7%)	1/27 (3.7%)	0/26 (0%)
# events				
Joint swelling † [A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Musculoskeletal pain † [A]				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# events				
Pain in extremity †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Nervous system disorders				
Headache †[A]				
# participants affected/at risk	11/27 (40.74%)	15/27 (55.56%)	15/27 (55.56%)	13/26 (50%)
# events				
Psychiatric disorders				
Insomnia †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Reproductive system and breast disorders				
Dysmenorrhoea †[A]				
# participants affected/at risk	2/27 (7.41%)	0/27 (0%)	1/27 (3.7%)	0/26 (0%)

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
# events				
Respiratory, thoracic and mediastinal disorders				
Bronchospasm †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Cough †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	0/27 (0%)	1/26 (3.85%)
# events				
Dry throat †[A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	1/27 (3.7%)	0/26 (0%)
# events				
Nasal dryness †[A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	0/27 (0%)	0/26 (0%)
# events				
Oropharyngeal pain †[A]				
# participants affected/at risk	2/27 (7.41%)	3/27 (11.11%)	2/27 (7.41%)	3/26 (11.54%)
# events				

	Placebo	FF/VI 100/25 µg OD	FF 100 µg OD	VI 25 µg OD
Rhinitis allergic † [A]				
# participants affected/at risk	0/27 (0%)	1/27 (3.7%)	1/27 (3.7%)	0/26 (0%)
# events				
Rhinorrhoea † [A]				
# participants affected/at risk	1/27 (3.7%)	1/27 (3.7%)	0/27 (0%)	1/26 (3.85%)
# events				
Throat irritation † [A]				
# participants affected/at risk	0/27 (0%)	0/27 (0%)	1/27 (3.7%)	1/26 (3.85%)
# events				
Skin and subcutaneous tissue disorders				
Eczema † [A]				
# participants affected/at risk	1/27 (3.7%)	1/27 (3.7%)	0/27 (0%)	1/26 (3.85%)
# events				
Ingrowing nail † [A]				
# participants affected/at risk	1/27 (3.7%)	0/27 (0%)	0/27 (0%)	0/26 (0%)
# 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: