Protocol Registration Receipt
07/10/2014

Grantor: CDER IND/IDE Number: 074696, 077855 Serial Number: 0052, 0051

A Study to Evaluate the Efficacy and Safety of Fluticasone Furoate (FF)/GW642444 Inhalation Powder 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:	NCT01009463

Purpose

The Purpose of this study is to assess the efficacy and safety of three strengths of the FF/GW642444 Inhalation Powder in subject with Chronic Obstructive Pulmonary Disease (COPD)

Condition	Intervention	Phase
Pulmonary Disease, Chronic Obstructive	Drug: FF/GW642444 Inhalation Powder	Phase 3

Condition	Intervention	Phase
	Drug: GW642444 Inhalation Powder	

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study
Official Title: HZC102871: A 52-week Efficacy and Safety Study to Compare the Effect of Three Dosage Strengths of Fluticasone Furoate/GW642444 Inhalation Powder With GW642444 on the Annual Rate of Exacerbations in Subjects With Chronic Obstructive Pulmonary Disease (COPD)

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean [Time Frame: From the start of the double blinded study medication until Visit 11 (Week 52)/Early Withdrawal] [Designated as safety issue: No]

  The annual rate of moderate and severe chronic obstructive pulmonary disease (COPD) exacerbations during the treatment (trt) period (per participant [par.] per year) was assessed. An exacerbation of COPD, is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least two consecutive days; or the worsening of any one major symptom together with any one of the minor symptoms (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. The COPD exacerbation was categorized as mild, moderate and severe by the investigator. Mild: worsening symptoms of COPD that were self-managed by the par. without the use of oral corticosteroids or antibiotics; Moderate: worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics; Severe: worsening symptoms of COPD that required treatment with in-patient hospitalization.

Secondary Outcome Measures:

- Time to First Occurrence of Moderate or Severe COPD Exacerbation [Time Frame: From the start of the double blind study medication until Visit 11 (Week 52)/Early Withdrawal] [Designated as safety issue: No]

  Time to first occurrence analyzed by using a Cox proportional hazards model with covariates of treatment, smoking status at screening (stratum), baseline disease severity (pre-dose Day 1 % predicted FEV1) and centre grouping. An exacerbation of COPD is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least two consecutive days; or the worsening of any one major symptom together with any one of the minor symptoms (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. A moderate exacerbation is defined as worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics. A severe exacerbation is defined as worsening symptoms of COPD that required treatment with in-patient hospitalization. The number of participants with a moderate or severe COPD exacerbation while on treatment are presented.
- Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean [Time Frame: From the start of the double blind study medication until Visit 11 (Week 52)/Early Withdrawal] [Designated as safety issue: No]

  The annual rate of COPD exacerbations during the treatment period (per participant per year) that required systemic/oral corticosteroids was assessed. An exacerbation of COPD is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least

two consecutive days; or the worsening of any one major symptom together with any one of the minor symptom (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. The COPD exacerbation was categorized as mild, moderate, and severe by the investigator. Mild: worsening symptoms of COPD that were self-managed by the participant. Mild exacerbations were not associated with the use of oral corticosteroids or antibiotics. Moderate: worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics. Severe: worsening symptoms of COPD that required treatment with in-patient hospitalization.

- Change From Baseline in Trough FEV1 at Week 52 (Visit 11) [Time Frame: Baseline to Visit 11 (Week 52)/Early Withdrawal] [Designated as safety issue: No]

  Pulmonary function was measured by forced expiratory volume in one second (FEV1). Trough FEV1 was defined as the 24-hour post-dose FEV1 assessment, which was obtained at each visit. Analysis performed using a repeated measures model with covariates of treatment, smoking status at Screening (stratum), baseline (pre-dose Day 1), centre grouping, Week, Week by Baseline, and Week by treatment interactions.

Enrollment: 1626
Study Start Date: September 2009
Study Completion Date: October 2011
Primary Completion Date: October 2011

Arms	Assigned Interventions
Experimental: FF/GW642444 Inhalation Powder 100/25 mcg QD Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA)	Drug: FF/GW642444 Inhalation Powder Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA) delivered within one dry powder inhaler (DPI) device for COPD
Experimental: FF/GW642444 Inhalation Powder 200/25 mcg QD Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA)	Drug: FF/GW642444 Inhalation Powder Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA) delivered within one dry powder inhaler (DPI) device for COPD
Experimental: FF/GW642444 Inhalation Powder 50mcg/25mcg QD Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA)	Drug: FF/GW642444 Inhalation Powder Inhaled Corticosteroid (ICS)/ Long Acting Beta Agonist(LABA) delivered within one dry powder inhaler (DPI) device for COPD
Experimental: GW642444 25mcg QD	Drug: GW642444 Inhalation Powder

Arms	Assigned Interventions
Long Acting Beta Agonist(LABA)	Long Acting Beta Agonist(LABA) Inhalation Powder via DPI

Eligibility

Ages Eligible for Study: 40 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- Type of subject: outpatient
- Informed consent: Subjects must give their signed and dated written informed consent to participate.
- Gender: Male or female subjects A female is eligible to enter and participate in the study if she is of: Non-child bearing potential (i.e., physiologically incapable of becoming pregnant, including any female who is post-menopausal or surgically sterile). Surgically sterile females are defined as those with a documented hysterectomy and/or bilateral oophorectomy or tubal ligation. Post-menopausal females are defined as being amenorrhoeic for greater than 1 year with an appropriate clinical profile, e.g., age appropriate, history of vasomotor symptoms. However in questionable cases, a blood sample with FSH > 40MIU/ml and estradiol <40pg/ml (<140 pmol/L) is confirmatory. OR

Child bearing potential, has a negative pregnancy test at screening, and agrees to one of the following acceptable contraceptive methods used consistently and correctly (i.e., in accordance with the approved product label and the instructions of the physician for the duration of the study – screening to follow-up contact):

- Complete abstinence from intercourse from screening until the Follow-Up Phone Contact; or
- Male partner is sterile (vasectomy with documentation of azoospermia) prior to female subject entry into the study, and this male partner is the sole partner for that subject; or
- Implants of levonorgestral inserted for at least 1 month prior to the study medication administration but not beyond the third successive year following insertion; or
- Injectable progestogen administered for at least 1 month prior to study medication administration and administered until the Follow-Up Phone Contact; or
- Oral contraceptive (combined or progestogen only) administered for at least one monthly cycle prior to study medication administration; or
- Double barrier method: condom or occlusive cap (diaphragm or cervical/vault caps) plus spermicidal agent (foam/gel/film/cream/suppository); or
- An intrauterine device (IUD), inserted by a qualified physician, with published data showing that the highest expected failure rate is less than 1% per year; or
- Estrogenic vaginal ring; or
- Percutaneous contraceptive patches
    - Age: ≥40 years of age at Screening (Visit 1)
    - COPD diagnosis: Subjects with a clinical history of COPD in accordance with the following definition by the American Thoracic Society/European

Respiratory Society [Celli, 2004]: COPD is a preventable and treatable disease characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.

- Tobacco use: Subjects with a current or prior history of ≥10 pack-years of cigarette smoking at Screening (Visit 1). Former smokers are defined as those who have stopped smoking for at least 6 months prior to Visit 1. Note: Pipe and/or cigar use cannot be used to calculate pack-year history. Number of pack years = (number of cigarettes per day/20) x number of years smoked
- Severity of Disease:

- Subject with a measured post-albuterol/salbutamol FEV1/FVC ratio of ≤0.70 at Screening (Visit 1)
- Subjects with a measured post-albuterol/salbutamol FEV1 <70% of predicted normal values calculated (via centralized vendor equipment) using NHANES III reference equations [Hankinson, 1999] at Screening (Visit 1). Post-bronchodilator spirometry will be performed approximately 10-15 minutes after the subject has self-administered 4 inhalations (i.e., total 400mcg) of albuterol/salbutamol via an MDI with a valved-holding chamber. The study provided central spirometry equipment will calculate the FEV1/FVC ratio and FEV1 percent predicted values.

- History of Exacerbations: A documented history (e.g., medical record verification) of at least one COPD exacerbation in the 12 months prior to Visit 1 that required either oral corticosteroids, antibiotics and/or hospitalization. Prior use of antibiotics alone does not qualify as an exacerbation history unless the use was associated with treatment of worsening symptoms of COPD, such as increased dyspnea, sputum volume, or sputum purulence (color). Subject verbal reports are not acceptable.

Exclusion Criteria:

Subjects meeting any of the following criteria must not be enrolled in the study:

- Pregnancy: Women who are pregnant or lactating or are planning on becoming pregnant during the study.
- Asthma: Subjects with a current diagnosis of asthma. (Subjects with a prior history of asthma are eligible if they have a current diagnosis of COPD)
- α1-antitrypsin deficiency: Subjects with α1-antitrypsin deficiency as the underlying cause of COPD
- Other respiratory disorders: Subjects with active tuberculosis, lung cancer, bronchiectasis, sarcoidosis, lung fibrosis, pulmonary hypertension, interstitial lung diseases or other active pulmonary diseases
- Lung resection: Subjects with lung volume reduction surgery within the 12 months prior to Screening (Visit 1)
- Chest X-ray (or CT scan): Subjects with a chest X-ray (or CT scan) that reveals evidence of clinically significant abnormalities not believed to be due to the presence of COPD. A chest X-ray must be taken at Screening (Visit 1) if a chest X-ray or CT scan is not available within 6 months prior to Visit 1. For sites in Germany, if a chest X-ray (or CT scan) is not available in the 6 months preceding Screening (Visit 1), the subject will not be eligible for the study.
- Risk Factors for Pneumonia: immune suppression (HIV, Lupus, etc) or other risk for pneumonia (e.g. neurological disorders affecting control of the upper airway, such as Parkinson’s, Myasthenia Gravis, etc).
- A moderate and severe COPD exacerbation that has not resolved at least 14 days prior to Visit 1 and at least 30 days following the last dose of oral corticosteroids (if applicable).
- Pneumonia and/or moderate and severe COPD exacerbation at Visit 1 Note: Subjects who experience a pneumonia and/or exacerbation at Screening (Visit

1) must be not continue in the study, but may be re-screened at a later time provided the pneumonia and/or COPD exacerbation has resolved prior to the re-screening visit. At the Re-screening Visit, the chest x-ray should confirm resolution of pneumonia. The Re-screening Visit must be conducted at least ≥ 14 days following the resolution date of the exacerbation and/or pneumonia and at least 30 days following the last dose of oral corticosteroids (if applicable).

- Other diseases/abnormalities: Subjects with historical or current evidence of clinically significant cardiovascular (i.e., pacemaker), neurological, psychiatric, renal, hepatic, immunological, endocrine (including uncontrolled diabetes or thyroid disease) or haematological abnormalities that are uncontrolled. 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.
- Peptic Ulcer disease: Subjects with clinically significant peptic ulcer disease that is uncontrolled.
- Hypertension: Subjects with clinically significant hypertension that is uncontrolled.
- Cancer: Subjects with carcinoma that has not been in complete remission for at least 5 years. Carcinoma in situ of the cervix, squamous cell carcinoma and basal cell carcinoma of the skin would not be excluded if the subject has been considered cured within 5 years since diagnosis.
- Drug/food allergy: Subjects with a history of hypersensitivity to any of the study medications (e.g., beta-agonists, corticosteroid) or components of the inhalation powder (e.g., lactose, magnesium stearate). In addition, subjects with a history of severe milk protein allergy that, in the opinion of the study physician, contraindicates the subject’s participation will also be excluded.
- Drug/alcohol abuse: Subjects with a known or suspected history of alcohol or drug abuse within the last 2 years
- Medication prior to spirometry: 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.
- Additional medication: Unable to stop using certain medications such as bronchodilators and corticosteroids for the protocol-specified times prior to Visit 1 (the Investigator will discuss the specific medications)
- Oxygen therapy: 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.
- Sleep apnea: Subjects with clinically significant sleep apnea who require use of continuous positive airway pressure (CPAP) device or non-invasive positive pressure ventilation (NIPPV) device.
- Pulmonary rehabilitation: Subjects who have participated in the acute phase of a Pulmonary Rehabilitation Program within 4 weeks prior to Screening (Visit 1) or who will enter the acute phase of a Pulmonary Rehabilitation Program during the study. Subjects who are in the maintenance phase of a Pulmonary Rehabilitation Program are not excluded.
- Non-compliance: Subjects at risk of non-compliance, or unable to comply with the study procedures. Any infirmity, disability, or geographic location that would limit compliance for scheduled visits.
- Questionable validity of consent: Subjects with a history of psychiatric disease, intellectual deficiency, poor motivation or other conditions that will limit the validity of informed consent to participate in the study.
- Prior use of study medication/other investigational drugs: Subjects who have previously been randomized to treatment with GW642444 Inhalation Powder in the B2C111045 study, randomized to treatment in the HZC111348 study or have participated in the HZC112207, HZC102871, HZC102970, or HZC110946 studies. Subjects who have received an investigational drug within 30 days of entry into this study (Screening), or within 5 drug half-lives of the investigational drug, whichever is longer.
- Affiliation with investigator site: 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.

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More Information

Publications:

Dransfield MT, Bourbeau J, Jones PW, Hanania NA, Mahler DA, Vestbo J, Wachtel A, Martinez FJ, Barnhart F, Sanford L, Lettis S, Crim C, Calverley PMA.

A once-daily inhaled corticosteroid, long-acting beta2-agonist combination, fluticasone furoate (FF) / vilanterol (VI), for the prevention of COPD exacerbations. Lancet Respir Med. 2013;1(3):210-223.

Responsible Party: GlaxoSmithKline
Study ID Numbers: 102871
Health Authority: United States: Food and Drug Administration

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Study Results

Participant Flow

Pre-Assignment Details

At Visit (V) 1, eligible participants (par.) entered a 4-week, open-label Run-In Period (RIP) to establish a stable Baseline. At V 2, eligible par. were randomized to a 52 week, double-blind Treatment Period. 2631 par. were screened, 2071 par. entered the RIP, and 1626 par. were randomized, out of which 1622 received at >= 1 study treatment dose.

Reporting Groups

	Description
FP/SAL 250/50 µg BID	Participants (Par.) were instructed to take open label Fluticasone Propionate and Salmeterol (FP/SAL) 250/50 microgram (µg) twice daily (BID) from the ACCUHALER/DISKUS, one inhalation each morning and evening with approximately 12 hours between doses. In addition, all par. were provided supplemental albuterol/salbutamol (metered dose inhaler [MDI] and/or nebules) to be used as needed throughout the study.
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

	Description
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

4-week, Open-label Run-In Period

	FP/SAL 250/50 µg BID	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Started	2071	0	0	0	0
Completed	1622	0	0	0	0
Not Completed	449	0	0	0	0
Did Not Meet Continuation Criteria	373	0	0	0	0
Adverse Event	10	0	0	0	0
Lost to Follow-up	6	0	0	0	0
Physician Decision	10	0	0	0	0

	FP/SAL 250/50 µg BID	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Withdrawal by Subject	50	0	0	0	0

52-week, Double-blind Treatment Period

	FP/SAL 250/50 µg BID	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Started	0	409	408	403	402
Completed the Treatment Period	0	295 [1]	318 [2]	314 [3]	303 [4]
Completed	0	294 [5]	315 [6]	312 [7]	301 [8]
Not Completed	0	115	93	91	101
Adverse Event	0	22	25	29	31
Withdrawal by Subject	0	34	18	17	22
Lack of Efficacy	0	24	16	11	18
Protocol Violation	0	8	7	8	7
Met Protocol-Defined Stopping Criteria	0	10	14	13	10
Study Closed/Terminated	0	2	0	1	0
Lost to Follow-up	0	11	7	6	5
Physician Decision	0	4	6	6	8

[1] Par. completed the treatment period if they attended the last treatment visit (Visit 11).

[2] Par. completed the treatment period if they attended the last treatment visit (Visit 11).

[3] Par. completed the treatment period if they attended the last treatment visit (Visit 11).

[4] Par. completed the treatment period if they attended the last treatment visit (Visit 11).

[5] Par. completed the study if they completed the treatment period and safety follow-up phone contact.

[6] Par. completed the study if they completed the treatment period and safety follow-up phone contact.

[7] Par. completed the study if they completed the treatment period and safety follow-up phone contact.

[8] Par. completed the study if they completed the treatment period and safety follow-up phone contact.

Baseline Characteristics

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

	Description
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Baseline Measures

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD	Total
Number of Participants	409	408	403	402	1622
Age, Continuous [units: Years] Mean (Standard Deviation)	63.6 (9.43)	63.6 (9.06)	63.6 (9.06)	63.8 (9.30)	63.6 (9.21)
Gender, Male/Female [units: Participants]					
Female	170	163	172	153	658
Male	239	245	231	249	964
Race/Ethnicity, Customized [units: participants]					
White	331	334	332	324	1321
African American/ African Heritage	9	8	6	9	32
Asian	39	37	37	41	154
American Indian or Alaska Native & White	19	16	19	15	69
Asian & White	0	1	0	0	1
American Indian or Alaska	10	12	9	12	43

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD	Total
Native					
Unknown	1	0	0	1	2

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean
Measure Description	The annual rate of moderate and severe chronic obstructive pulmonary disease (COPD) exacerbations during the treatment (trt) period (per participant [par.] per year) was assessed. An exacerbation of COPD, is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least two consecutive days; or the worsening of any one major symptom together with any one of the minor symptoms (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. The COPD exacerbation was categorized as mild, moderate and severe by the investigator. Mild: worsening symptoms of COPD that were self-managed by the par. without the use of oral corticosteroids or antibiotics; Moderate: worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics; Severe: worsening symptoms of COPD that required treatment with in-patient hospitalization.
Time Frame	From the start of the double blinded study medication until Visit 11 (Week 52)/Early Withdrawal
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all par. randomized who received at least 1 dose of study drug and with available data for analysis. Analysis used a negative binomial regression model with covariates of trt, smoking status at Screening, Baseline pre-dose Day 1 % predicted FEV1 and region and with logarithm of time on trt as an offset variable.

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Measured Values

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Number of Participants Analyzed	409	408	403	402

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean [units: Exacerbations per participant per year] Least Squares Mean (95% Confidence Interval)	1.05 (0.92 to 1.21)	0.92 (0.80 to 1.06)	0.70 (0.60 to 0.81)	0.90 (0.78 to 1.04)

Statistical Analysis 1 for Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 50/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	0.181
Risk Ratio (RR)	0.87
95% Confidence Interval	0.72 to 1.06

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:

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable.

Statistical Analysis 2 for Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 100/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	<0.001
Risk Ratio (RR)	0.66

95% Confidence Interval	0.54 to 0.81

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:

Nominal p-value

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

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable.

Statistical Analysis 3 for Annual Rate of Moderate and Severe COPD Exacerbations Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 200/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	0.109
Risk Ratio (RR)	0.85
95% Confidence Interval	0.70 to 1.04

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:

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable.

2. Secondary Outcome Measure:

Measure Title	Time to First Occurrence of Moderate or Severe COPD Exacerbation

Measure Description	Time to first occurrence analyzed by using a Cox proportional hazards model with covariates of treatment, smoking status at screening (stratum), baseline disease severity (pre-dose Day 1 % predicted FEV1) and centre grouping. An exacerbation of COPD is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least two consecutive days; or the worsening of any one major symptom together with any one of the minor symptoms (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. A moderate exacerbation is defined as worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics. A severe exacerbation is defined as worsening symptoms of COPD that required treatment with in-patient hospitalization. The number of participants with a moderate or severe COPD exacerbation while on treatment are presented.
Time Frame	From the start of the double blind study medication until Visit 11 (Week 52)/Early Withdrawal
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.)
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of

	Description
	the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Measured Values

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Number of Participants Analyzed	409	408	403	402
Time to First Occurrence of Moderate or Severe COPD Exacerbation [units: Participants]	202	190	160	178

Statistical Analysis 1 for Time to First Occurrence of Moderate or Severe COPD Exacerbation

Groups	VI 25 µg QD, FF/VI 50/25 µg QD
Method	Regression, Cox
P-Value	0.430
Hazard Ratio (HR)	0.92
95% Confidence Interval	0.76 to 1.13

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.]

Statistical Analysis 2 for Time to First Occurrence of Moderate or Severe COPD Exacerbation

Groups	VI 25 µg QD, FF/VI 100/25 µg QD
Method	Regression, Cox
P-Value	0.002
Hazard Ratio (HR)	0.72
95% Confidence Interval	0.59 to 0.89

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:

Nominal p-value

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

[Not specified.]

Statistical Analysis 3 for Time to First Occurrence of Moderate or Severe COPD Exacerbation

Groups	VI 25 µg QD, FF/VI 200/25 µg QD
Method	Regression, Cox
P-Value	0.114
Hazard Ratio (HR)	0.85

95% Confidence Interval	0.69 to 1.04

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.]

3. Secondary Outcome Measure:

Measure Title	Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean
Measure Description	The annual rate of COPD exacerbations during the treatment period (per participant per year) that required systemic/oral corticosteroids was assessed. An exacerbation of COPD is defined as the worsening of two or more major symptoms (dyspnea, sputum volume, sputum purulence [color]) for at least two consecutive days; or the worsening of any one major symptom together with any one of the minor symptom (sore throat, cold, fever without other cause, increased cough, increased wheeze) for at least two consecutive days. The COPD exacerbation was categorized as mild, moderate, and severe by the investigator. Mild: worsening symptoms of COPD that were self-managed by the participant. Mild exacerbations were not associated with the use of oral corticosteroids or antibiotics. Moderate: worsening symptoms of COPD that required treatment with oral corticosteroids and/or antibiotics. Severe: worsening symptoms of COPD that required treatment with in-patient hospitalization.
Time Frame	From the start of the double blind study medication until Visit 11 (Week 52)/Early Withdrawal

Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all par. randomized who received at least 1 dose of study drug and with available data for analysis. Analysis used a negative binomial regression model with covariates of trt, smoking status at Screening, Baseline pre-dose Day 1 % predicted FEV1 and region and with logarithm of time on trt as an offset variable.

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Measured Values

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Number of Participants Analyzed	409	408	403	402
Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean [units: Exacerbations per participant per year] Least Squares Mean (95% Confidence Interval)	0.84 (0.72 to 0.98)	0.71 (0.60 to 0.83)	0.52 (0.44 to 0.62)	0.68 (0.57 to 0.80)

Statistical Analysis 1 for Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 50/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	0.125
Risk Ratio (RR)	0.84
95% Confidence Interval	0.67 to 1.05

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:

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable.

Statistical Analysis 2 for Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 100/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	<0.001

Risk Ratio (RR)	0.62
95% Confidence Interval	0.49 to 0.78

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:

Nominal p-value

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

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable

Statistical Analysis 3 for Annual Rate of Exacerbations Requiring Systemic/Oral Corticosteroids Expressed as Least Square Mean

Groups	VI 25 µg QD, FF/VI 200/25 µg QD
Method	Other [Generalized Linear Model]
P-Value	0.064
Risk Ratio (RR)	0.81
95% Confidence Interval	0.64 to 1.01

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:

Assuming Negative Binomial distribution with logarithm of time on treatment as an offset variable

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Trough FEV1 at Week 52 (Visit 11)
Measure Description	Pulmonary function was measured by forced expiratory volume in one second (FEV1). Trough FEV1 was defined as the 24-hour post-dose FEV1 assessment, which was obtained at each visit. Analysis performed using a repeated measures model with covariates of treatment, smoking status at Screening (stratum), baseline (pre-dose Day 1), centre grouping, Week, Week by Baseline, and Week by treatment interactions.
Time Frame	Baseline to Visit 11 (Week 52)/Early Withdrawal
Safety Issue?	No

Analysis Population Description

ITT Population. Number of participants presented represent those with data available at the time point being presented, however all participants in the ITT population without missing covariate information and with at least one post Baseline measurement are included in the analysis.

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the

	Description
	morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Measured Values

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Number of Participants Analyzed	291	308	310	289
Change From Baseline in Trough FEV1 at Week 52 (Visit 11) [units: Liters] Least Squares Mean (Standard Error)	-0.040 (0.0114)	0.000 (0.0112)	0.018 (0.0112)	0.024 (0.0114)

Statistical Analysis 1 for Change From Baseline in Trough FEV1 at Week 52 (Visit 11)

Groups	VI 25 µg QD, FF/VI 50/25 µg QD
Method	Mixed Models Analysis
P-Value	0.011
Other Estimated Parameter [Least squares mean difference]	0.041
95% Confidence Interval	0.009 to 0.072

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:

Nominal p-value

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

Restricted maximum likelihood (REML)-based repeated measures approach (MMRM).

Statistical Analysis 2 for Change From Baseline in Trough FEV1 at Week 52 (Visit 11)

Groups	VI 25 µg QD, FF/VI 100/25 µg QD
Method	Mixed Models Analysis
P-Value	<0.001
Other Estimated Parameter [Least squares mean difference]	0.058
95% Confidence Interval	0.027 to 0.090

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:

Nominal p-value

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

Restricted maximum likelihood (REML)-based repeated measures approach (MMRM).

Statistical Analysis 3 for Change From Baseline in Trough FEV1 at Week 52 (Visit 11)

Groups	VI 25 µg QD, FF/VI 200/25 µg QD
Method	Mixed Models Analysis
P-Value	<0.001
Other Estimated Parameter [Least squares mean difference]	0.064

95% Confidence Interval	0.033 to 0.096

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:

Nominal p-value

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

Restricted maximum likelihood (REML)-based repeated measures approach (MMRM).

Reported Adverse Events

Reporting Groups

	Description
VI 25 µg QD	Participants received a Vilanterol (VI) 25 µg dry inhalation powder once daily (QD) in the morning from the Dry Powder Inhaler (DPI) for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 50/25 µg QD	Participants received a Fluticasone Furoate/Vilanterol (FF/VI) 50/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.
FF/VI 100/25 µg QD	Participants received a FF/VI 100/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

	Description
FF/VI 200/25 µg QD	Participants received a FF/VI 200/25 µg inhalation powder QD in the morning from the DPI for the duration of the 52 weeks. In addition, all participants were provided supplemental albuterol/salbutamol (MDI and/or nebules) to be used as needed throughout the study.

Time Frame

Serious adverse events (SAEs) and non-serious AEs will be collected from Baseline to the end of the treatment period (up to 52 weeks).

Additional Description

SAEs and non-serious adverse events are reported for members of the Intent-to-Treat Population, comprised of all randomized participants who received at least one dose of study medication during the treatment period.

Serious Adverse Events

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Total # participants affected/at risk	60/409 (14.67%)	65/408 (15.93%)	56/403 (13.9%)	63/402 (15.67%)
Blood and lymphatic system disorders				
Anaemia † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	1/402 (0.25%)
# events				
Cardiac disorders				
Acute coronary syndrome † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	1/409 (0.24%)	1/408 (0.25%)	1/403 (0.25%)	0/402 (0%)
# events				
Acute myocardial infarction † [A]				
# participants affected/at risk	1/409 (0.24%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Angina pectoris † [A]				
# participants affected/at risk	1/409 (0.24%)	2/408 (0.49%)	0/403 (0%)	0/402 (0%)
# events				
Angina unstable † [A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Arrhythmia † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Atrial fibrillation † [A]				
# participants affected/at risk	1/409 (0.24%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Cardiac arrest † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Cardiac failure † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Cardiac failure congestive † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Cardio-respiratory arrest † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Coronary artery stenosis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Coronary artery thrombosis				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
† [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Myocardial infarction † [A]				
# participants affected/at risk	1/409 (0.24%)	2/408 (0.49%)	2/403 (0.5%)	2/402 (0.5%)
# events				
Palpitations † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Supraventricular tachycardia † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Eye disorders				
Diplopia † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Gastrointestinal				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
disorders				
AE Term: Salivary gland enlargement † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Abdominal pain † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Abdominal pain lower † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Abdominal strangulated hernia † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Constipation † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Diverticulum intestinal †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Gastric ulcer haemorrhage †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Gastritis †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Gastritis erosive †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Gastrointestinal haemorrhage †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Gastrooesophageal reflux disease †[A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Haemorrhoids † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Hiatus hernia † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Ileus † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Melaena † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Rectal haemorrhage † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Small intestinal obstruction †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Upper gastrointestinal haemorrhage †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
General disorders				
Chest pain †[A]				
# participants affected/at risk	1/409 (0.24%)	2/408 (0.49%)	0/403 (0%)	0/402 (0%)
# events				
Death †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Non-cardiac chest pain †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Hepatobiliary disorders				
Bile duct obstruction † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Bile duct stone † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Cholecystitis † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Immune system disorders				
Anaphylactic shock † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Infections and infestations				
Arthritis bacterial † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Bone tuberculosis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Bronchitis † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	2/402 (0.5%)
# events				
Bronchopneumonia † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	1/402 (0.25%)
# events				
Cellulitis † [A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	4/403 (0.99%)	0/402 (0%)
# events				
Clostridium difficile colitis † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Escherichia sepsis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Gastroenteritis viral † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
H1N1 influenza † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Infective exacerbation of chronic obstructive airway disease † [A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	2/403 (0.5%)	0/402 (0%)
# events				
Lobar pneumonia † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	1/402 (0.25%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Lower respiratory tract infection † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Lung abscess † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	1/402 (0.25%)
# events				
Mycobacterium avium complex infection † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Pneumonia † [A]				
# participants affected/at risk	2/409 (0.49%)	12/408 (2.94%)	9/403 (2.23%)	12/402 (2.99%)
# events				
Pulmonary tuberculosis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Pyelonephritis acute † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Respiratory tract infection † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Septic shock † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Tuberculosis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Upper respiratory tract infection † [A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Urinary tract infection † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Urinary tract infection bacterial †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Injury, poisoning and procedural complications				
Fall †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Foot fracture †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Head injury †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Hip fracture †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Laceration † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Operative haemorrhage † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Pneumothorax traumatic † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Spinal compression fracture † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Toxicity to various agents † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Wrist fracture † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Metabolism and nutrition disorders				
Diabetes mellitus inadequate control † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Hyperglycaemia † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	2/403 (0.5%)	0/402 (0%)
# events				
Hypokalaemia † [A]				
# participants affected/at risk	2/409 (0.49%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Hyponatraemia † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Hypovolaemia †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Ketoacidosis †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Musculoskeletal and connective tissue disorders				
Arthritis reactive †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Back pain †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Bursitis †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Costochondritis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Intervertebral disc protrusion † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Joint stiffness † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Musculoskeletal chest pain † [A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Osteoarthritis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Neoplasms benign,				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
malignant and unspecified (incl cysts and polyps)				
Acute lymphocytic leukaemia †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Brain cancer metastatic †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Breast cancer †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Colon cancer †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Laryngeal cancer †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Lung cancer metastatic † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Lung neoplasm malignant † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Malignant hepatobiliary neoplasm † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Malignant melanoma † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Metastases to bone † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Metastases to liver † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Metastases to lung † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Metastatic carcinoma of the bladder † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Non-Hodgkin's lymphoma † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Pancreatic carcinoma metastatic † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	1/402 (0.25%)
# events				
Small cell carcinoma † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Squamous cell carcinoma † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	2/402 (0.5%)
# events				
Nervous system disorders				
Carotid artery aneurysm † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Carotid artery stenosis † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Cerebrovascular accident † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	2/403 (0.5%)	3/402 (0.75%)
# events				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Convulsion †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Dizziness †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Loss of consciousness †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Metabolic encephalopathy †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Syncope †[A]				
# participants affected/at risk	2/409 (0.49%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Psychiatric disorders				
Depression †[A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Depression suicidal †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Renal and urinary disorders				
Calculus urinary †[A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Haematuria †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Renal failure acute †[A]				
# participants affected/at risk	0/409 (0%)	3/408 (0.74%)	0/403 (0%)	0/402 (0%)
# events				
Urethral stenosis †[A]				
# participants affected/at	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
risk				
# events				
Reproductive system and breast disorders				
Benign prostatic hyperplasia †[A]				
# participants affected/at risk	2/409 (0.49%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Respiratory, thoracic and mediastinal disorders				
Acute pulmonary oedema †[A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Acute respiratory failure †[A]				
# participants affected/at risk	0/409 (0%)	3/408 (0.74%)	3/403 (0.74%)	2/402 (0.5%)
# events				
Asthma †[A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Bronchitis chronic † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Bronchopleural fistula † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)
# events				
Chronic obstructive pulmonary disease † [A]				
# participants affected/at risk	28/409 (6.85%)	27/408 (6.62%)	26/403 (6.45%)	30/402 (7.46%)
# events				
Hypoxia † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Pleural effusion † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	2/403 (0.5%)	0/402 (0%)
# events				
Pneumothorax † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	2/402 (0.5%)
# events				
Pulmonary embolism † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Pulmonary oedema † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Respiratory failure † [A]				
# participants affected/at risk	0/409 (0%)	2/408 (0.49%)	0/403 (0%)	0/402 (0%)
# events				
Vocal cord disorder † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Vascular disorders				
Aortic aneurysm rupture † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	0/403 (0%)	1/402 (0.25%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Haematoma † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Hypertension † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	1/402 (0.25%)
# events				
Hypertensive crisis † [A]				
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (0%)
# events				
Peripheral arterial occlusive disease † [A]				
# participants affected/at risk	0/409 (0%)	0/408 (0%)	1/403 (0.25%)	0/402 (0%)
# events				
Shock † [A]				
# participants affected/at risk	1/409 (0.24%)	0/408 (0%)	0/403 (0%)	0/402 (0%)
# events				
Shock haemorrhagic † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	0/409 (0%)	1/408 (0.25%)	0/403 (0%)	0/402 (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%

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
Total # participants affected/at risk	197/409 (48.17%)	227/408 (55.64%)	221/403 (54.84%)	225/402 (55.97%)
Gastrointestinal disorders				
Diarrhoea † [A]				
# participants affected/at risk	15/409 (3.67%)	12/408 (2.94%)	8/403 (1.99%)	15/402 (3.73%)
# events				
Nausea † [A]				
# participants affected/at risk	10/409 (2.44%)	24/408 (5.88%)	7/403 (1.74%)	10/402 (2.49%)
# events				
General disorders				
Pyrexia † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	5/409 (1.22%)	17/408 (4.17%)	10/403 (2.48%)	8/402 (1.99%)
# events				
Infections and infestations				
Bronchitis †[A]				
# participants affected/at risk	20/409 (4.89%)	13/408 (3.19%)	21/403 (5.21%)	23/402 (5.72%)
# events				
Influenza †[A]				
# participants affected/at risk	21/409 (5.13%)	10/408 (2.45%)	13/403 (3.23%)	13/402 (3.23%)
# events				
Nasopharyngitis †[A]				
# participants affected/at risk	54/409 (13.2%)	58/408 (14.22%)	60/403 (14.89%)	76/402 (18.91%)
# events				
Oral candidiasis †[A]				
# participants affected/at risk	21/409 (5.13%)	39/408 (9.56%)	34/403 (8.44%)	36/402 (8.96%)
# events				
Oropharyngeal candidiasis †[A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	2/409 (0.49%)	14/408 (3.43%)	7/403 (1.74%)	6/402 (1.49%)
# events				
Pharyngitis † [A]				
# participants affected/at risk	14/409 (3.42%)	8/408 (1.96%)	14/403 (3.47%)	16/402 (3.98%)
# events				
Pneumonia † [A]				
# participants affected/at risk	10/409 (2.44%)	17/408 (4.17%)	16/403 (3.97%)	16/402 (3.98%)
# events				
Rhinitis † [A]				
# participants affected/at risk	6/409 (1.47%)	9/408 (2.21%)	10/403 (2.48%)	15/402 (3.73%)
# events				
Sinusitis † [A]				
# participants affected/at risk	17/409 (4.16%)	21/408 (5.15%)	22/403 (5.46%)	13/402 (3.23%)
# events				
Upper respiratory tract infection † [A]				
# participants affected/at risk	45/409 (11%)	47/408 (11.52%)	51/403 (12.66%)	39/402 (9.7%)

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# events				
Urinary tract infection † [A]				
# participants affected/at risk	7/409 (1.71%)	16/408 (3.92%)	10/403 (2.48%)	17/402 (4.23%)
# events				
Musculoskeletal and connective tissue disorders				
Arthralgia † [A]				
# participants affected/at risk	13/409 (3.18%)	13/408 (3.19%)	16/403 (3.97%)	13/402 (3.23%)
# events				
Back pain † [A]				
# participants affected/at risk	30/409 (7.33%)	21/408 (5.15%)	24/403 (5.96%)	20/402 (4.98%)
# events				
Nervous system disorders				
Dizziness † [A]				
# participants affected/at risk	8/409 (1.96%)	13/408 (3.19%)	5/403 (1.24%)	3/402 (0.75%)
# events				
Headache † [A]				

	VI 25 µg QD	FF/VI 50/25 µg QD	FF/VI 100/25 µg QD	FF/VI 200/25 µg QD
# participants affected/at risk	30/409 (7.33%)	27/408 (6.62%)	25/403 (6.2%)	34/402 (8.46%)
# events				
Respiratory, thoracic and mediastinal disorders				
Cough †[A]				
# participants affected/at risk	14/409 (3.42%)	21/408 (5.15%)	16/403 (3.97%)	13/402 (3.23%)
# events				
Dyspnoea †[A]				
# participants affected/at risk	10/409 (2.44%)	13/408 (3.19%)	6/403 (1.49%)	4/402 (1%)
# events				
Oropharyngeal pain †[A]				
# participants affected/at risk	13/409 (3.18%)	7/408 (1.72%)	14/403 (3.47%)	13/402 (3.23%)
# events				
Vascular disorders				
Hypertension †[A]				
# participants affected/at risk	6/409 (1.47%)	15/408 (3.68%)	19/403 (4.71%)	12/402 (2.99%)
# 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:

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