ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: October 25, 2012

ClinicalTrials.gov ID: NCT00527826

Study Identification

Unique Protocol ID:	SCO107227
Brief Title:	Influence Of Salmeterol Xinafoate/Fluticasone Propionate (50/500 µg BID) On The Course Of The Disease And Exacerbation Frequency In COPD Patients Gold Stage III And IV
Official Title:	A 12 Month Open-label Randomized Parallel Group Study to Investigate the Influence of Salmeterol Xinafoate/Fluticasone Propionate Either in Fixed Combination or Separately Via Diskus Inhalers on the Course of the Disease and Frequency of Exacerbations in Subjects With Severe and Very Severe COPD.
Secondary IDs:	

Study Status

Record Verification:	October 2012
Overall Status:	Completed
Study Start:	November 2007 []
Primary Completion:	July 2009 [Actual]
Study Completion:	July 2009 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:

U.S. FDA-regulated Device:

U.S. FDA IND/IDE: No

Human Subjects Review: Board Status: Approved
Approval Number: SCO107227
Board Name: Ethik-Kommission der Landesarztekammer Hessen
Board Affiliation: Ethik-Kommission der Landesarztekammer Schleswig-Holstein
Phone: +49-(0)69-976720
Email: info@laekh.de
Address:

Frankfurt, N/A, 60488, Germany

Data Monitoring:

FDA Regulated Intervention: No

Study Description

Brief Summary: This is a 12 month randomized, open-label, parallel-group study to obtain data on the frequency and variability of exacerbations in severe and very severe Chronic Obstructive Pulmonary Disease (COPD) patients (Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stage III and IV) receiving salmeterol xinafoate and fluticasone propionate either in fixed combination (SFC) or from separate inhalers (Sal/FP) with standard therapy. 200 subjects will be enrolled in approximately 30 study centres in Germany. Data on health care utilisation will be collected to compare direct costs associated with COPD in these two groups.

Baseline data will be collected for all subjects at Visit 1 and eligible subjects will be randomized to receive either SFC 50/500 µg bid (twice daily) as fixed combination or Sal 50 µg bid (twice daily) and FP 500 µg bid (twice daily) concurrently over 52 weeks. Subjects will return for study visits every two to three months until week 52. Additional telephone calls will be made between scheduled visits every 4 weeks. Assessments will include monitoring of frequency of exacerbations, health care utilisation (including emergency visits and hospitalizations) and rescue medication, lung function, drug compliance, health-related quality of life (SGRQ = St George's Respiratory Questionnaire) and safety.

Detailed Description: A 12 month open-label randomized parallel group study to investigate the influence of salmeterol xinafoate/fluticasone propionate either in fixed combination (SFC50/500 µg bid) or separately (SAL 50 µg and FP 500 µg bid) via Diskus inhalers on the course of the disease and frequency of exacerbations in subjects with severe and very severe COPD (GOLD stage III+IV)

Conditions

Conditions: Pulmonary Disease, Chronic Obstructive

Keywords: Severe and very severe COPD (GOLD stage III / IV) exacerbations

health care utilisation
Chronic Obstructive Pulmonary Disease (COPD)
quality of life
compliance
salmeterol/fluticasone combination

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Interventional Study Model:	Parallel Assignment
Number of Arms:	2
Masking:	None (Open Label)
Allocation:	Randomized
Enrollment:	214 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: arm 1	Drug: Salmeterol / Fluticasone (50/500 µg) BID fixed combination comparator
Active Comparator: arm 2	Drug: Salmeterol / Fluticasone (50/500 µg) BID separate Inhalers comparator

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	40 Years
Maximum Age:	
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	No

Criteria: Inclusion criteria:

- Subject must have a diagnosis of COPD based on the American Thoracic Society (ATS)/ European Respiratory Society (ERS) criteria.
- Male or female subjects, aged >=40 years. Females must be of Non Child Bearing Potential. The definition of Non Child Bearing Potential is as following: Females, regardless of their age, with functioning ovaries and who have a current documented tubal ligation or hysterectomy, or females who are post-menopausal.
- Have diagnosed COPD stage III or IV according to GOLD criteria: a baseline post-bronchodilator Forced Expiratory Volume, measured at 1 second (FEV1) <50% of predicted normal and a baseline post- bronchodilator FEV1/Inspiratory Vital Capacity (IVC) ratio <70%.
- Have experienced at least 2 moderate or severe COPD exacerbations leading to medical consultation (requiring oral corticosteroids or increasing dosage of oral corticosteroids and/or antibiotics or hospitalization) within the 12 months preceding Visit 1.
- Have stable COPD medication within 4 weeks prior to Visit 1 (no new medication added and no dosage changes in medication).
- Current or ex-smokers with a smoking history of at least 10 pack years (number of pack years = [number of cigarettes per day / 20] x number of years smoked, e.g., 20 cigarettes per day for 10 years, or 10 cigarettes per day for 20 years).
- Are currently managed at home (outpatients), are ambulatory and able to travel to the clinic. Subjects can be treated with all relevant COPD medication. This includes vaccines, inhaled short-acting beta-2-agonists as needed, short-acting or long-acting anticholinergics (tiotropium), systemic beta-2-agonists, theophylline, mucolytics, antioxidants, beta-1-agonists (for cardiovascular indication), non-invasive ventilation, long term oxygen therapy and can have Cor Pulmonale.
- A signed and dated written informed consent is obtained prior to participation.
- Able to comply with the requirements of the protocol and be available for study visits over 52 weeks.

Exclusion criteria:

- Known other respiratory disorders or signs for other respiratory disorders (e.g. asthma, lung cancer, sarcoidosis, tuberculosis, lung fibrosis, cystic fibrosis, bronchoectasis).
- Known history of significant inflammatory disease, other than COPD (e.g. rheumatoid arthritis and systemic lupus erythematosus).
- Known to be severely alpha-1-antitrypsin deficient (PI SZ or ZZ)
- Having undergone lung surgery (e.g. lung resection including lung volume reduction surgery, lung transplant) or subjects scheduled for surgery.
- Concurrent medication from Visit 1 and for the duration of the study with any of the prohibited medications: monoamine oxidase inhibitors and tricyclic antidepressants, and ritonavir (a highly potent cytochrome P450 3A4 inhibitor).
- Subjects receiving chronic or prophylactic antibiotic therapy.
- Serious, uncontrolled disease (including serious psychological disorders) likely to interfere with the study or impact on subject safety.
- Have, in the opinion of the investigator, evidence of alcohol, drug or solvent abuse.
- History of depression.
- History or presence of clinically significant drug sensitivity or clinically significant allergic reaction to corticosteroids or salmeterol.
- Moderate or severe COPD exacerbation (requiring corticosteroids or increased dosage of corticosteroids and/or antibiotics or hospitalization) within the 4 weeks prior to Visit 1
- Lower respiratory tract infection within the 4 weeks prior to Visit 1 .
- Pregnant or lactating female and female of childbearing potential.

- Subject is a participating investigator, sub-investigator, study coordinator, or other employee of a participating investigator, or is an immediate family member of the before mentioned. Subject is an employee of GlaxoSmithKline (GSK).
- Subject participated in an investigational drug study within 30 days prior to Visit 1

Contacts/Locations

Central Contact Person: US GSK Clinical Trials Call Center
Telephone: 877-379-3718
Email: GSKClinicalSupportHD@gsk.com

Central Contact Backup:

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations: Germany

GSK Investigational Site
Annaberg, Sachsen, Germany, 09456
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Hamburg, Germany, 22299
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Berlin, Germany, 13187
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Berlin, Germany, 10365
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Bochum, Nordrhein-Westfalen, Germany, 44787
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Wiesbaden, Hessen, Germany, 65183
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com

Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Marburg, Hessen, Germany, 35037
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Gelnhausen, Hessen, Germany, 63571
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Wiesloch, Baden-Wuerttemberg, Germany, 69168
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Saarbruecken, Saarland, Germany, 66111
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Leipzig, Sachsen, Germany, 04275
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Schmoelln, Thueringen, Germany, 04626
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Neuruppin, Brandenburg, Germany, 16816
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Hannover, Niedersachsen, Germany, 30169
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Guetersloh, Nordrhein-Westfalen, Germany, 33330
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Kassel, Hessen, Germany, 34121
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Bruchsal, Baden-Wuerttemberg, Germany, 76646
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Eschwege, Hessen, Germany, 37269
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Heidelberg, Baden-Wuerttemberg, Germany, 69117
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Cottbus, Brandenburg, Germany, 03050
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Potsdam, Brandenburg, Germany, 14469
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Radebeul, Sachsen, Germany, 01445
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Kassel, Hessen, Germany, 34121
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

GSK Investigational Site
Mannheim, Baden-Wuerttemberg, Germany, 68161
Contact: US GSK Clinical Trials Call Center 877-379-3718 GSKClinicalSupportHD@gsk.com
Contact: EU GSK Clinical Trials Call Center +44 (0) 20 8990 4466 GSKClinicalSupportHD@gsk.com

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)

Overall Study

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
Started	108 [1]	106
Completed	87	80
Not Completed	21	26
Adverse Event	10	10
Lost to Follow-up	3	2
Withdrawal by Subject	5	8

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
Inclusion Criteria Not Met	3	3
Alpha-1 Antitrypsin Deficiency	0	1
Additional Intake of Viani forte	0	1
Participant moved away	0	1

[1] All Patients Population was used for Participant Flow section.

Baseline Characteristics

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)

Baseline Measures

		Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Total
Overall Number of Participants		107	105	212
Age, Continuous [1] Mean (Standard Deviation) Unit of measure: years	Number Analyzed	107 participants	105 participants	212 participants
		65.6 (8.3)	64.2 (8.9)	64.9 (8.6)
		[1] Measure Description: Age at study start (years). The Intent-to-Treat (ITT) Population (all participants receiving at least one dose of study medication and suffering from COPD) was used for all baseline characteristics.		

		Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Total
Sex: Female, Male [1] Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	107 participants	105 participants	212 participants
	Female	33 30.84%	29 27.62%	62 29.25%
	Male	74 69.16%	76 72.38%	150 70.75%
	[1] Measure Description: The ITT Population was used.			
Severity of Chronic Obstructive Lung Disease (COPD) [1] Measure Type: Number Unit of measure: participants	Number Analyzed	107 participants	105 participants	212 participants
Severe COPD		77	79	156
Very severe COPD		30	26	56
	[1] Measure Description: Severe COPD (stage III) is defined by the global initiative for chronic obstructive lung disease (GOLD) as baseline forced expiratory volume in one second (FEV1) >30% and <50% predicted and FEV1/inspiratory vital capacity (IVC) ratio <70%. Very severe COPD (stage IV) is defined as baseline FEV1 <30% predicted and FEV1/IVC <70%. ITT Population.			
Smoking History [1] Measure Type: Number Unit of measure: participants	Number Analyzed	107 participants	105 participants	212 participants
Ex-smoker		74	78	152
Smoker		33	27	60
	[1] Measure Description: The number of smokers/ex-smokers participating in the study was recorded. The ITT Population was used.			

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Mean Number of Exacerbations Per Year: Negative Binomial Model
Measure Description	During regular visits, participants were asked whether they experienced any exacerbation since last contact. Between visits, COPD participants were contacted by phone by the staff and asked about exacerbation details. Exacerbations were defined according to Rodriguez-Roisin: moderate (grade II) exacerbations include a worsening of COPD symptoms that require both a change of respiratory medication (increased dose of prescribed or addition of new drugs) and medical assistance; severe (grade III) exacerbations include deterioration in COPD resulting in hospitalization or emergency room treatment.
Time Frame	Baseline through Week 52

Analysis Population Description

Intent-to-Treat (ITT) Population: all participants receiving at least one dose of study medication and suffering from COPD

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)

Measured Values

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
Overall Number of Participants Analyzed	107	105
Mean Number of Exacerbations Per Year: Negative Binomial Model Least Squares Mean (Standard Error) Unit of measure: Number of exacerbations per year	0.864 (0.134)	0.862 (0.138)

Statistical Analysis 1 for Mean Number of Exacerbations Per Year: Negative Binomial Model

Statistical Analysis Overview	Comparison Group Selection	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg, Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Comments	[Not specified]

	Type of Statistical Test	Non-Inferiority or Equivalence (legacy)
	Comments	Negative binomial model for the rate of exacerbations (per year) using the treatment duration as offset term and treatment, COPD severity (stratum) and interaction as fixed factors. This model took further into account a strata imbalance of 73% COPD III vs. 27% COPD IV according to the observed rates (SAS code: proc GENMOD).

Statistical Test of Hypothesis	P-Value	0.73
	Comments	[Not specified]
	Method	Other [Negative binomial model]
	Comments	Least square means adjusted for COPD severity (stratum), interaction of stratum with treatment, and strata imbalance of 73% COPD III vs. 27% COPD IV.

2. Primary Outcome Measure:

Measure Title	Mean Number of Exacerbations Per Year: Poisson Model
Measure Description	During regular visits, participants were asked whether they experienced any exacerbation since last contact. Between visits, COPD participants were contacted by phone by the staff and asked about exacerbation details. Exacerbations were defined according to Rodriguez-Roisin: moderate (grade II) exacerbations include a worsening of COPD symptoms that require both a change of respiratory medication (increased dose of prescribed or addition of new drugs) and medical assistance; severe (grade III) exacerbations include deterioration in COPD resulting in hospitalization or emergency room treatment.
Time Frame	Baseline through Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)

Measured Values

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
Overall Number of Participants Analyzed	107	105

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
Mean Number of Exacerbations Per Year: Poisson Model Least Squares Mean (Standard Error) Unit of measure: Number of exacerbations per year	0.863 (0.136)	0.830 (0.137)

Statistical Analysis 1 for Mean Number of Exacerbations Per Year: Poisson Model

Statistical Analysis Overview	Comparison Group Selection	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg, Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Comments	[Not specified]
	Type of Statistical Test	Non-Inferiority or Equivalence (legacy)
	Comments	Poisson model for the rate of exacerbations (per year) using the treatment duration as offset term and treatment, COPD severity (stratum) and interaction as fixed factors. This model took further into account a strata imbalance of 73% COPD III vs. 27% COPD IV according to the observed rates (SAS code: proc GENMOD).

Statistical Test of Hypothesis	P-Value	0.66
	Comments	[Not specified]
	Method	Other [Poisson model]
	Comments	Least square means adjusted for COPD severity (stratum), interaction of stratum with treatment, and strata imbalance of 73% COPD III vs. 27% COPD IV.

3. Secondary Outcome Measure:

Measure Title	Compliance and Adherence to Study Medication
Measure Description	Compliance is calculated as the ratio (in percent) between the number of actual doses taken during the total treatment period divided by the number of doses that should have been taken during the total treatment period.
Time Frame	Baseline through Week 52

Analysis Population Description

ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Sal 50 µg	Salmeterol xinafoate (Sal) 50 µg BID (morning and evening) from a separate inhaler (SEVERENT Diskus)
FP 500 µg	Fluticasone propionate (FP) 500 µg BID (morning and evening) from a separate inhaler (FLUTIDE forte Diskus)

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Sal 50 µg	FP 500 µg
Overall Number of Participants Analyzed	107	105	105
Compliance and Adherence to Study Medication Mean (Standard Deviation) Unit of measure: percentage of doses	97.08 (11.61)	98.44 (19.62)	98.33 (19.36)

4. Secondary Outcome Measure:

Measure Title	Mean Number of COPD-related Visits at/by Physician
Measure Description	The total number of COPD-related visits, i.e., from baseline through week 52, the number of visits at physician's office, the number of home visits made by physician, the number of visits at an emergency outpatient clinic, as well as the number of home visits by an emergency physician were summed up.
Time Frame	Baseline through Week 52

Analysis Population Description

ITT Population with non-missing data (due to early withdrawal some data for this outcome measure are missing)

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	98	96	194
Mean Number of COPD-related Visits at/by Physician Mean (Standard Deviation) Unit of measure: number of visits	1.39 (2.33)	1.06 (2.23)	1.23 (2.28)

5. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Number of Days at the Intensive Care Unit (ICU)
Measure Description	The number participants with the indicated number of days at the ICU was recorded.
Time Frame	Baseline through Week 52

Analysis Population Description

ITT Population of participants who were admitted to the ICU

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	25	16	41
Number of Participants With the Indicated Number of Days at the Intensive Care Unit (ICU) Measure Type: Number Unit of measure: participants			

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
0 days	19	13	32
1-5 days	4	2	6
6-10 days	1	1	2
11-30 days	0	0	0
>30 days	1	0	1

6. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Number of Hospital Stays
Measure Description	The number of participants with the indicated number of hospitalizations was recorded.
Time Frame	Baseline through Week 52

Analysis Population Description

ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Number of Participants With the Indicated Number of Hospital Stays Measure Type: Number Unit of measure: participants			
0 hospital stays	82	87	169
1 hospital stay	11	13	24
2 hospital stays	9	3	12
3 hospital stays	4	1	5
4 hospital stays	0	1	1
5 or more hospital stays	1	0	1

7. Secondary Outcome Measure:

Measure Title	Mean Number of Days Rescue Medication Was Used
Measure Description	Participants were asked for the number of days they used rescue medication within the 7 days before Week 8 and Week 52.
Time Frame	The 7 days before baseline (=Visit 2 [Week 8]) and the last 7 days of study (=Visit 6 [Week 52])

Analysis Population Description

ITT Population with non-missing data (due to early withdrawal, some data for this outcome measure are missing).

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	101	98	199
Mean Number of Days Rescue Medication Was Used Mean (Standard Deviation) Unit of measure: number of days			
Visit 2 (Week 8)	4.73 (2.37)	4.11 (2.77)	4.43 (2.58)
Final visit (Week 52)	5.03 (2.45)	4.69 (2.67)	4.86 (2.56)

8. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Week 52
Measure Description	Change from baseline was calculated as the FEV1 percent predicted value at Week 52 minus the percent predicted value at baseline. The post-bronchodilator lung function test was performed to measure FEV1 30 minutes after inhaling salbutamol. The most reliable result of three different consecutive measurements was documented.
Time Frame	Baseline and Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Mean Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Week 52 Mean (Standard Deviation) Unit of measure: percent of predicted value			
Baseline	36.82 (8.93)	38.15 (9.26)	37.47 (9.10)
Week 52	38.98 (13.15)	41.22 (15.26)	40.09 (14.24)
Mean change from baseline	2.17 (10.42)	3.08 (12.08)	2.62 (11.26)

9. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in Inspiratory Vital Capacity (IVC) at Week 52
Measure Description	Change from baseline was measured as the IVC value at Week 52 minus the value at baseline. The post-bronchodilator lung function test was performed to measure IVC 30 minutes after inhaling salbutamol. The most reliable result of three different, consecutive measurements was documented.
Time Frame	Baseline and Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Mean Change From Baseline in Inspiratory Vital Capacity (IVC) at Week 52 Mean (Standard Deviation) Unit of measure: liters			
Baseline	2.17 (0.74)	2.29 (0.71)	2.23 (0.72)
Week 52	2.14 (0.72)	2.27 (0.68)	2.21 (0.70)
Mean change from baseline	-0.02 (0.53)	-0.02 (0.50)	-0.02 (0.51)

10. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the Tiffeaneau Index at Week 52
Measure Description	The Tiffeneau index is defined as the FEV1 divided by the IVC (i.e., forced expiratory volume in one second relative to the inspiratory capacity) in percent. Change from baseline is calculated as the FEV1/IVC value at Week 52 minus the value at baseline.
Time Frame	Baseline and Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Mean Change From Baseline in the Tiffeaneau Index at Week 52 Mean (Standard Deviation) Unit of measure: percent of IVC			
Baseline	48.90 (11.09)	49.05 (10.76)	48.98 (10.90)
Week 52	50.82 (10.98)	52.83 (16.39)	51.81 (13.93)
Mean change from baseline	1.92 (8.76)	3.78 (13.42)	2.84 (11.32)

11. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the Symptom Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52
Measure Description	Change from baseline is calculated as the symptom score at Week 52 minus the symptom score at baseline. The SGRQ (a self-administered questionnaire) subscale symptom score ranges from 0 to 100% and measures the effect of respiratory symptoms, frequency, and severity on quality of life (summed weights of 8 questions). A score of 0 indicates the best possible status.
Time Frame	Baseline and Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212
Mean Change From Baseline in the Symptom Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52 Mean (Standard Deviation) Unit of measure: percent			
Baseline	68.80 (19.65)	68.95 (18.38)	68.88 (18.99)
Week 52	65.42 (19.76)	63.77 (19.94)	64.61 (19.82)
Mean change from baseline	-3.38 (17.65)	-5.18 (17.27)	-4.27 (17.44)

12. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the Activity Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52
Measure Description	Change from baseline is calculated as the activity score at Week 52 minus the score at baseline. The SGRQ (a self-administered questionnaire) subscale activity score ranges from 0 to 100% and is concerned with activities that cause or are limited by breathlessness (summed weights of 2 questions). A score of 0 indicates the best possible status.
Time Frame	Baseline and Week 52

Analysis Population Description

ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212
Mean Change From Baseline in the Activity Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52 Mean (Standard Deviation) Unit of measure: percent			
Baseline	72.80 (17.78)	70.64 (17.45)	71.73 (17.61)
Week 52	71.17 (20.29)	68.53 (21.72)	69.86 (21.01)
Mean change from baseline	-1.63 (16.63)	-2.11 (16.53)	-1.87 (16.54)

13. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the Impact Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52
Measure Description	Change from baseline was calculated as the impact score at Week 52 minus the score at baseline. The SGRQ (a self-administered questionnaire) subscale impact score ranges from 0 to 100% and is concerned with social functioning and psychological disturbances (summed weights of 5 questions). A score of 0 indicates the best possible status.
Time Frame	Baseline and Week 52

Analysis Population Description

ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	112
Mean Change From Baseline in the Impact Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52 Mean (Standard Deviation) Unit of measure: percent			
Baseline	46.03 (20.30)	43.58 (17.37)	44.82 (18.90)
Week 52	44.66 (21.15)	41.26 (19.53)	42.98 (20.39)
Mean change from baseline	-1.37 (17.52)	-2.32 (17.87)	-1.84 (17.66)

14. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the Total Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52
Measure Description	Change from baseline was calculated as the total score at Week 52 minus the score at baseline. The SGRQ (a self-administered questionnaire) total score ranges from 0 to 100% and summarizes the impact of COPD on overall health status (summed weights of 15 questions). A total score of 0 indicates the best possible status.
Time Frame	Baseline and Week 52

Analysis Population Description

ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212
Mean Change From Baseline in the Total Score of the St. George's Respiratory Questionnaire (SGRQ) at Week 52 Mean (Standard Deviation) Unit of measure: percent			
Baseline	57.82 (17.07)	55.89 (15.36)	56.87 (16.24)
Week 52	56.02 (18.22)	53.25 (17.71)	54.65 (17.98)
Mean change from baseline	-1.80 (14.42)	-2.64 (14.73)	-2.22 (14.55)

15. Secondary Outcome Measure:

Measure Title	Mean Total Costs (Related to COPD) Per Participant
Measure Description	Total costs include costs for hospitalization, medication, and visits to/by physician. Medications that were used "as required" were assumed to be used every second day.
Time Frame	Baseline through Week 52

Analysis Population Description
ITT Population

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)
Total	Total number of participants randomized to the SFC and Sal/FP groups

Measured Values

	Salmeterol Xinafoate/ FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/ FP Separately (Sal/ FP) 50/500 µg	Total
Overall Number of Participants Analyzed	107	105	212
Mean Total Costs (Related to COPD) Per Participant Mean (Standard Deviation) Unit of measure: Euros per participant	1453 (2427)	1166 (1534)	1311 (2034)

Reported Adverse Events

Time Frame	Adverse events (AE) and serious adverse events (SAEs) were collected after the start of the study (visit 1, Week 0) until the last visit (visit 6, Week 52).
Adverse Event Reporting Description	The Safety Population (all participants who took at least one dose of study medication) was used for the analysis of SAEs/AEs. One participant in the Sal/FP group was excluded from the safety population because (s)he took no study medication (returned the study medication unused).

Reporting Groups

	Description
Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol xinafoate/fluticasone propionate (FP) 50/500 µg twice a day (BID) (morning and evening) from the fixed combination inhaler (VIANI forte Diskus)
Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg	Salmeterol xinafoate (Sal)/fluticasone propionate (FP) 50/500 µg BID (morning and evening) from two separate inhalers (SEREVENT Diskus and FLUTIDE forte Diskus)

All-Cause Mortality

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Affected/At Risk (%)	Affected/At Risk (%)
Total All-Cause Mortality	/	/

Serious Adverse Events

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	23/108 (21.3%)	16/105 (15.24%)
Blood and lymphatic system disorders		
Anaemia [A] †	1/108 (0.93%)	0/105 (0%)
Cardiac disorders		
Arrhythmia [A] †	0/108 (0%)	1/105 (0.95%)
Atrial fibrillation [A] †	0/108 (0%)	1/105 (0.95%)
Cardiac failure [A] †	1/108 (0.93%)	1/105 (0.95%)
Cyanosis [A] †	0/108 (0%)	1/105 (0.95%)
Tachyarrhythmia [A] †	1/108 (0.93%)	0/105 (0%)
Gastrointestinal disorders		
Diarrhoea [A] †	1/108 (0.93%)	0/105 (0%)
Duodenal stenosis [A] †	1/108 (0.93%)	0/105 (0%)
Duodenitis [A] †	1/108 (0.93%)	0/105 (0%)
Gastric ulcer [A] †	0/108 (0%)	1/105 (0.95%)
Gastritis [A] †	1/108 (0.93%)	0/105 (0%)
Gastrointestinal haemorrhage [A] †	0/108 (0%)	1/105 (0.95%)
Haemorrhoids [A] †	1/108 (0.93%)	0/105 (0%)
Intestinal haemorrhage [A] †	0/108 (0%)	1/105 (0.95%)
General disorders		
Chest pain [A] †	1/108 (0.93%)	0/105 (0%)
Pain [A] †	0/108 (0%)	1/105 (0.95%)
Infections and infestations		

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Affected/At Risk (%)	Affected/At Risk (%)
Infective exacerbation of chronic obstructive airways disease [A] †	2/108 (1.85%)	1/105 (0.95%)
Pneumonia [A] †	3/108 (2.78%)	4/105 (3.81%)
Injury, poisoning and procedural complications		
Concussion [A] †	1/108 (0.93%)	0/105 (0%)
Rib fracture [A] †	1/108 (0.93%)	0/105 (0%)
Musculoskeletal and connective tissue disorders		
Back pain [A] †	1/108 (0.93%)	0/105 (0%)
Intervertebral disc protrusion [A] †	1/108 (0.93%)	1/105 (0.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] †	1/108 (0.93%)	0/105 (0%)
Bladder neoplasm [A] †	0/108 (0%)	1/105 (0.95%)
Breast cancer [A] †	1/108 (0.93%)	0/105 (0%)
Bronchial carcinoma [A] †	1/108 (0.93%)	0/105 (0%)
Laryngeal cancer [A] †	1/108 (0.93%)	0/105 (0%)
Nervous system disorders		
Cervicobrachial syndrome [A] †	1/108 (0.93%)	0/105 (0%)
Syncope [A] †	1/108 (0.93%)	0/105 (0%)
Transient ischaemic attack [A] †	1/108 (0.93%)	0/105 (0%)
Renal and urinary disorders		
Renal failure [A] †	0/108 (0%)	1/105 (0.95%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia [A] †	1/108 (0.93%)	0/105 (0%)

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure [A] †	0/108 (0%)	1/105 (0.95%)
Chronic obstructive pulmonary disease [A] †	12/108 (11.11%)	7/105 (6.67%)
Dyspnoea [A] †	0/108 (0%)	1/105 (0.95%)
Pulmonary embolism [A] †	0/108 (0%)	1/105 (0.95%)
Surgical and medical procedures		
Cardioplegia [A] †	0/108 (0%)	1/105 (0.95%)
Vascular disorders		
Arterial occlusive disease [A] †	1/108 (0.93%)	0/105 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Salmeterol Xinafoate/FP in Fixed Combination (SFC) 50/500 µg	Salmeterol Xinafoate/FP Separately (Sal/FP) 50/500 µg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	45/108 (41.67%)	48/105 (45.71%)
Infections and infestations		
Infective exacerbation of chronic obstructive airways disease [A] †	12/108 (11.11%)	16/105 (15.24%)
Nasopharyngitis [A] †	3/108 (2.78%)	8/105 (7.62%)
Pneumonia [A] †	7/108 (6.48%)	5/105 (4.76%)
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease [A] †	33/108 (30.56%)	33/105 (31.43%)
Dyspnoea [A] †	4/108 (3.7%)	6/105 (5.71%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

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.

Results Point of Contact:

Name/Official Title: GSK Response Center
Organization: GlaxoSmithKline
Phone: 866-435-7343
Email: