ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/10/2012

ClinicalTrials.gov ID: NCT00496470

Study Identification

Unique Protocol ID:	D5892C00015
Brief Title:	Evaluation of Efficacy and Safety of Symbicort® as an add-on Treatment to Spiriva® in Patients With Severe COPD.
Official Title:	A 12-week, Double-blind, Randomised, Parallel Group, Multi-centre, Study to Evaluate Efficacy and Safety of Budesonide/ Formoterol (Symbicort Turbuhaler®) 320/9 µg One Inhalation Twice Daily on Top of Tiotropium (Spiriva®) 18 µg One Inhalation Once Daily
Secondary IDs:	Eudract no:2006-006796-21

Study Status

Record Verification:	October 2012
Overall Status:	Completed
Study Start:	May 2007
Primary Completion:	June 2008 [Actual]
Study Completion:	June 2008 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 7281-1/2007-1017EKL Board Name: Medical Research Council Ethics Committee for Clinical Pharmacology Board Affiliation: ... Phone: +36 1 301 7871 Email: magyari.ilona@eum.hu
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Australia: Department of Health and Ageing Therapeutic Goods Administration France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Germany: Federal Institute for Drugs and Medical Devices Hungary: National Institute of Pharmacy Poland: Ministry of Health Slovakia: State Institute for Drug Control Canada: Canadian Institutes of Health Research Spain: Spanish Agency of Medicines Sweden: Medical Products Agency

Study Description

Brief Summary:	The purpose of this study is to investigate the effect of combined treatment with Symbicort and Spiriva, in terms of improvement of lung function, symptoms and inflammatory markers, in patients with severe COPD.
Detailed Description:	

Conditions

Conditions:	Chronic Obstructive Pulmonary Disease, COPD
Keywords:	Chronic Obstructive Pulmonary Disease, COPD

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4

Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Efficacy Study
Enrollment:	660 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Symbicort+TIO Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily	Drug: Symbicort (budesonide/formoterol turbuhaler 320/9ug) Symbicort (budesonide/formoterol turbuhaler 320/9ug)
Active Comparator: Spiriva® + Placebo Turbuhaler Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily	Drug: Spiriva (tiotropium bromide 18ug) Spiriva (tiotropium bromide 18ug)

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	40 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- >=40 years of age, diagnosed COPD with symptoms >=2 years, pre-bronchodilatory FEV1 <=50% of PN

Exclusion Criteria:

- Current respiratory tract disorder other than COPD, history of asthma or rhinitis, significant or unstable cardiovascular disorder

Contacts/Locations

Study Officials: Tomas Andersson, MD
Study Director
AstraZeneca R&D Lund

Tobias Welte, MD
Study Principal Investigator
Medizinische Hochschule Hannover

Locations: Australia, New South Wales
Research Site
Concord, New South Wales, Australia

Research Site
Sydney, New South Wales, Australia

Australia, Queensland
Research Site
Auchenflower, Queensland, Australia

Research Site
Carina Heights, Queensland, Australia

Research Site
North Mackay, Queensland, Australia

Australia, South Australia
Research Site
Adelaide, South Australia, Australia

Research Site
Daw Park, South Australia, Australia

Australia, Victoria
Research Site
Clayton, Victoria, Australia

Research Site
Malvern, Victoria, Australia

Australia, Western Australia
Research Site
Nedlands, Western Australia, Australia

Canada, Alberta
Research Site
Calgary, Alberta, Canada

Canada, British Columbia
Research Site
Vancouver, British Columbia, Canada

Canada, Manitoba
Research Site
Winnipeg, Manitoba, Canada

Canada, Newfoundland and Labrador
Research Site
St. John's, Newfoundland and Labrador, Canada

Canada, Nova Scotia
Research Site
Halifax, Nova Scotia, Canada

Canada, Ontario
Research Site
Mississauga, Ontario, Canada

Research Site
Toronto, Ontario, Canada

Canada
Research Site
Quebec, Canada

Canada, Quebec
Research Site
La Malbaie, Quebec, Canada

Research Site
Trois-rivires, Quebec, Canada

Canada, Saskatchewan
Research Site
Saskatoon, Saskatchewan, Canada

France
Research Site
Chamalieres, France

Research Site
Creil, France

Research Site
Ferolles Attilly, France

Research Site
Grasse, France

Research Site
Lille, France

Research Site
Marseille Cedex 06, France

Research Site
Metz, France

Research Site
Montpellier, France

Research Site
Perpignan, France

Research Site
Poitiers Cedex, France

Research Site
Selestat, France

Research Site
St Laurent Du Var, France

Research Site
Strasbourg Cedex, France

Research Site
Toulouse Cedex 9, France

Germany
Research Site
Berlin, Germany

Research Site
Gelsenkirchen, Germany

Research Site
Hagen, Germany

Research Site
Hannover, Germany

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Kassel, Germany

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Koblenz, Germany

Research Site
Leipzig, Germany

Research Site
Marburg, Germany

Research Site
Potsdam, Germany

Hungary
Research Site
Aszod, Hungary

Research Site
Baja, Hungary

Research Site
Balassagyarmat, Hungary

Research Site
Budapest, Hungary

Research Site
Cegled, Hungary

Research Site
Debrecen, Hungary

Research Site
Fuzesabony, Hungary

Research Site
Jaszbereny, Hungary

Research Site
Komlo, Hungary

Research Site
Nyiregyhaza, Hungary

Research Site
Torokbalint, Hungary

Research Site
Vásárosnamény, Hungary

Poland
Research Site
Bydgoszcz, Poland

Research Site
Chrzanów, Poland

Research Site
Ilawa, Poland

Research Site
Krakow, Poland

Research Site
Lomza, Poland

Research Site
Piekary Slaskie, Poland

Research Site
Tarnow, Poland

Research Site
Turek, Poland

Research Site
Zawadzkie, Poland

Slovakia
Research Site
Kosice, Slovakia

Research Site
Liptovsky Hradok, Slovakia

Research Site
Lucenec, Slovakia

Research Site
Nove Mesto Nad Vahom, Slovakia

Research Site
Nove Zamky, Slovakia

Research Site
Piestany, Slovakia

Research Site
Poprad, Slovakia

Research Site
Povazska Bystrica, Slovakia

Research Site
Presov, Slovakia

Research Site
Prievidza, Slovakia

Research Site
Revuca, Slovakia

Research Site
Trnava, Slovakia

Research Site
Zilina, Slovakia

Spain
Research Site
Barcelona, Cataluna, Spain

Research Site
Reus (tarragona), Cataluna, Spain

Research Site
Madrid, Comunidad de Madrid, Spain

Research Site
Requena (valencia), Comunidad Valenciana, Spain

Research Site
Valencia, Comunidad Valenciana, Spain

Research Site
Pontevedra, Galicia, Spain

Sweden
Research Site
Lindesberg, Orebro Lan, Sweden

Research Site
Atvidaberg, Sweden

Research Site
Hollviken, Sweden

Research Site
Limhamn, Sweden

Research Site
Lund, Sweden

Research Site
Malmo, Sweden

Research Site
Motala, Sweden

Research Site
Stockholm, Sweden

Research Site
Uppsala, Sweden

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Overall Study

	Symbicort+Tiotropium	Placebo+Tiotropium
Started	329	331
Received Study Medication	329	330
Completed	303	302
Not Completed	26	29
Adverse Event	8	10
Withdrawal by Subject	5	12
Incorrectly enrolled	13	5
Other reason	0	2

Baseline Characteristics

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Baseline Measures

	Symbicort+Tiotropium	Placebo+Tiotropium	Total
Number of Participants	329	331	660

	Symbicort+Tiotropium	Placebo+Tiotropium	Total
Age, Continuous [units: Years] Mean (Full Range)	62.4 (40 to 85)	62.5 (41 to 82)	62.45 (40 to 85)
Gender, Male/Female [units: Participants]			
Female	78	86	164
Male	251	245	496

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Forced Expiratory Volume in 1 Second (FEV1) Pre-dose
Measure Description	Change in the pre-dose FEV1from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	323	327
Forced Expiratory Volume in 1 Second (FEV1) Pre-dose [units: Liters] Mean (Standard Deviation)	0.064 (0.198)	-0.001 (0.168)

2. Secondary Outcome Measure:

Measure Title	Forced Expiratory Volume in 1 Second (FEV1) 5 Min Post-dose
Measure Description	Change in the 5 min post-dose FEV1from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Forced Expiratory Volume in 1 Second (FEV1) 5 Min Post-dose [units: Liters] Mean (Standard Deviation)	0.165 (0.184)	0.042 (0.14)

3. Secondary Outcome Measure:

Measure Title	Forced Expiratory Volume in 1 Second (FEV1) 60 Min Post-dose
Measure Description	Change in the 60 min post-dose FEV1from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Forced Expiratory Volume in 1 Second (FEV1) 60 Min Post-dose [units: Liters] Mean (Standard Deviation)	0.214 (0.209)	0.083 (0.157)

4. Secondary Outcome Measure:

Measure Title	Forced Vital Capacity (FVC) Pre-dose
Measure Description	Change in the pre-dose FVC from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	323	327
Forced Vital Capacity (FVC) Pre-dose [units: Liters] Mean (Standard Deviation)	0.07 (0.341)	0.014 (0.348)

5. Secondary Outcome Measure:

Measure Title	Forced Vital Capacity (FVC) 5 Minutes Post-dose
Measure Description	Change in the 5 min post-dose FVC from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Forced Vital Capacity (FVC) 5 Minutes Post-dose [units: Liters] Mean (Standard Deviation)	0.266 (0.32)	0.106 (0.296)

6. Secondary Outcome Measure:

Measure Title	Forced Vital Capacity (FVC) 60 Minutes Post-dose
Measure Description	Change in the 60 min post-dose FVC from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Forced Vital Capacity (FVC) 60 Minutes Post-dose [units: Liters] Mean (Standard Deviation)	0.353 (0.357)	0.19 (0.319)

7. Secondary Outcome Measure:

Measure Title	Inspiratory Capacity (IC) Pre-dose
Measure Description	Change in the pre-dose IC from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	314	309
Inspiratory Capacity (IC) Pre-dose [units: Liters] Mean (Standard Deviation)	0.078 (0.35)	0.014 (0.389)

8. Secondary Outcome Measure:

Measure Title	Inspiratory Capacity (IC) 60 Minutes Post-dose
Measure Description	Change in the 60 min post-dose IC from baseline to week 12 (calculated as a mean using all available data of treatment period between week 1 and week 12)
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	318	310
Inspiratory Capacity (IC) 60 Minutes Post-dose	0.26 (0.353)	0.149 (0.359)

	Symbicort+Tiotropium	Placebo+Tiotropium
[units: Liters] Mean (Standard Deviation)		

9. Secondary Outcome Measure:

Measure Title	St George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Score
Measure Description	Change in total score from baseline (Visit 3) to end of treatment (Visit 6, or last available visit). SGRQ-C is a health related quality of life questionnaire consisting of 40 items divided into two components: 1) symptoms, 2) activity& impacts. The lowest possible value is zero and the highest 100. Higher values correspond to greater impairment in quality of life.
Time Frame	Baseline and 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	315	320
St George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Score [units: Score on a scale] Mean (Standard Deviation)	-4.12 (12.81)	-1.99 (12.77)

10. Secondary Outcome Measure:

Measure Title	Morning Peak Expiratory Flow (PEF) Pre-dose

Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Morning Peak Expiratory Flow (PEF) Pre-dose [units: Liters/minute] Mean (Standard Deviation)	5.12 (38.3)	-3.52 (24.7)

11. Secondary Outcome Measure:

Measure Title	Evening Peak Expiratory Flow (PEF) Pre-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
Evening Peak Expiratory Flow (PEF) Pre-dose [units: Liters/minute] Mean (Standard Deviation)	2.82 (37.6)	-5.54 (28.9)

12. Secondary Outcome Measure:

Measure Title	Morning Peak Expiratory Flow (PEF) 5 Min Post-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	294	307
Morning Peak Expiratory Flow (PEF) 5 Min Post-dose [units: Liters/minute]	16.71 (42.6)	1.1 (26.5)

	Symbicort+Tiotropium	Placebo+Tiotropium
Mean (Standard Deviation)		

13. Secondary Outcome Measure:

Measure Title	Morning Peak Expiratory Flow (PEF) 15 Min Post-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	293	311
Morning Peak Expiratory Flow (PEF) 15 Min Post-dose [units: Liters/minute] Mean (Standard Deviation)	20.4 (43.7)	5.2 (28.3)

14. Secondary Outcome Measure:

Measure Title	Morning Diary FEV1 Pre-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks

Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	219	233
Morning Diary FEV1 Pre-dose [units: Liters] Mean (Standard Deviation)	0.054 (0.201)	-0.046 (0.185)

15. Secondary Outcome Measure:

Measure Title	Evening Diary FEV1, Pre-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	221	237
Evening Diary FEV1, Pre-dose [units: Liters] Mean (Standard Deviation)	0.012 (0.223)	-0.065 (0.249)

16. Secondary Outcome Measure:

Measure Title	Morning Diary FEV1, 5 Minutes Post-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	191	205
Morning Diary FEV1, 5 Minutes Post-dose [units: Liters] Mean (Standard Deviation)	0.169 (0.224)	-0.018 (0.189)

17. Secondary Outcome Measure:

Measure Title	Morning Diary FEV1, 15 Minutes Post-dose

Measure Description	Daily diary record. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	190	208
Morning Diary FEV1, 15 Minutes Post-dose [units: Liters] Mean (Standard Deviation)	0.209 (0.236)	0.014 (0.201)

18. Secondary Outcome Measure:

Measure Title	Global Chest Symptoms Questionnaire (GCSQ) Score, Pre-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. The GCSQ consisted of two questions that required the patient to rate shortness of breath and feelings of chest tightness. The patients recorded their response on a five-point Likert-type scale ranging from 0 (not at all) to 4 (extremely), the total score being calculated as the average score of the two questions.
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	328
Global Chest Symptoms Questionnaire (GCSQ) Score, Pre-dose [units: Scores on a scale] Mean (Standard Deviation)	-0.143 (0.453)	-0.006 (0.438)

19. Secondary Outcome Measure:

Measure Title	GCSQ Score, 5 Minutes Post-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. The GCSQ consisted of two questions that required the patient to rate shortness of breath and feelings of chest tightness. The patients recorded their response on a five-point Likert-type scale ranging from 0 (not at all) to 4 (extremely), the total score being calculated as the average score of the two questions.
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	296	305
GCSQ Score, 5 Minutes Post-dose [units: Scores on a scale] Mean (Standard Deviation)	-0.325 (0.508)	-0.202 (0.46)

20. Secondary Outcome Measure:

Measure Title	GCSQ Score, 15 Minutes Post-dose
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. The GCSQ consisted of two questions that required the patient to rate shortness of breath and feelings of chest tightness. The patients recorded their response on a five-point Likert-type scale ranging from 0 (not at all) to 4 (extremely), the total score being calculated as the average score of the two questions.
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	293	309
GCSQ Score, 15 Minutes Post-dose [units: Scores on a scale] Mean (Standard Deviation)	-0.404 (-0.526)	-0.28 (-0.501)

21. Secondary Outcome Measure:

Measure Title	Capacity of Day Living in the Morning (CDLM) Score
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. The CDLM questionnaire is as a questionnaire to report on patient's ability to carry out each of six different morning activities (score ranging from 0 "not performed" to 1"performed") and rank the difficulty of performing each of those activities (score ranging from 0 "so difficult that the activity could not be carried out by the patient on their own" to 5 "activity was not at all difficult to carry out". Total score for each morning activity range from 0-6. Total score for whole CDLM questionnaire range from 0-36.
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	281	294
Capacity of Day Living in the Morning (CDLM) Score [units: Scores on a scale] Mean (Standard Deviation)	0.202 (0.467)	0.07 (0.435)

22. Secondary Outcome Measure:

Measure Title	Use of Rescue Medication, Night
Measure Description	Daily diary record - Night, after evening measurement till morning. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Use of Rescue Medication, Night [units: Inhalations] Mean (Standard Deviation)	-0.279 (0.7)	0.022 (0.743)

23. Secondary Outcome Measure:

Measure Title	Use of Rescue Medication, Morning
Measure Description	Daily diary record - Morning, after morning measurement till midday. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	281	294
Use of Rescue Medication, Morning [units: Inhalations] Mean (Standard Deviation)	-0.417 (0.758)	-0.124 (0.877)

24. Secondary Outcome Measure:

Measure Title	Use of Rescue Medication, Day
Measure Description	Daily diary record - Day, after morning measurement till evening. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
Use of Rescue Medication, Day [units: Inhalations] Mean (Standard Deviation)	-0.745 (1.286)	-0.371 (1.622)

25. Secondary Outcome Measure:

Measure Title	Use of Rescue Medication, Total
Measure Description	Daily diary record - Total, 24 hours, during the night, and during the day. Change in average values from run-in to the full treatment period
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
Use of Rescue Medication, Total [units: Inhalations] Mean (Standard Deviation)	-1.024 (1.704)	-0.347 (2.102)

26. Secondary Outcome Measure:

Measure Title	COPD Symptoms, Breathing Score
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. Symptom scale 0 - 4 (0) None (1) Mild (2) Moderate (3) Marked (4) Severe
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
COPD Symptoms, Breathing Score [units: Units on a Scale] Mean (Standard Deviation)	-0.177 (0.503)	-0.049 (0.5)

27. Secondary Outcome Measure:

Measure Title	COPD Symptoms, Sleeping Score
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. Symptom scale 0 - 4 (0) None (1) Mild (2) Moderate (3) Marked (4) Severe
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
COPD Symptoms, Sleeping Score	-0.197 (0.45)	-0.045 (0.462)

	Symbicort+Tiotropium	Placebo+Tiotropium
[units: Units on a Scale] Mean (Standard Deviation)		

28. Secondary Outcome Measure:

Measure Title	COPD Symptoms, Chest Score
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. Symptom scale 0 - 4 (0) None (1) Mild (2) Moderate (3) Marked (4) Severe
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
COPD Symptoms, Chest Score [units: Units on a Scale] Mean (Standard Deviation)	-0.184 (0.5)	-0.061 (0.473)

29. Secondary Outcome Measure:

Measure Title	COPD Symptoms, Cough Score
Measure Description	Daily diary record. Change in average values from run-in to the full treatment period. Symptom scale 0 - 4 (0) None (1) Mild (2) Moderate (3) Marked (4) Severe

Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	329
COPD Symptoms, Cough Score [units: Units on a Scale] Mean (Standard Deviation)	-0.246 (0.567)	-0.079 (0.545)

30. Secondary Outcome Measure:

Measure Title	Severe COPD Exacerbations
Measure Description	Patients with worsening of COPD leading to treatment with systemic steroids (oral or parenteral), emergency room treatment or hospitalisation
Time Frame	12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily

	Description
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	329	330
Severe COPD Exacerbations [units: Participants]	25	61

31. Secondary Outcome Measure:

Measure Title	Serum High-sensitivity C-reactive Protein (hsCRP)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum High-sensitivity C-reactive Protein (hsCRP) [units: Ratio] Median (Inter-Quartile Range)	0.91 (0.5 to 1.76)	0.97 (0.6 to 1.54)

32. Secondary Outcome Measure:

Measure Title	Serum Interleukin 6 (IL-6)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Interleukin 6 (IL-6) [units: Ratio] Median (Inter-Quartile Range)	1.0 (0.72 to 1.56)	1.0 (0.67 to 1.56)

33. Secondary Outcome Measure:

Measure Title	Serum Interleukin 8 (IL-8)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Interleukin 8 (IL-8) [units: Ratio] Median (Inter-Quartile Range)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)

34. Secondary Outcome Measure:

Measure Title	Serum Monocyte Chemoattractant Protein-1 (MCP-1)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Monocyte Chemoattractant Protein-1 (MCP-1) [units: Ratio]	0.95 (0.78 to 1.15)	0.95 (0.79 to 1.11)

	Symbicort+Tiotropium	Placebo+Tiotropium
Median (Inter-Quartile Range)		

35. Secondary Outcome Measure:

Measure Title	Serum Soluble Tumor Necrosis Factor-alpha (sTNF-alpha)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Soluble Tumor Necrosis Factor-alpha (sTNF-alpha) [units: Ratio] Median (Inter-Quartile Range)	0.97 (0.85 to 1.08)	0.98 (0.88 to 1.1)

36. Secondary Outcome Measure:

Measure Title	Serum Tumor Necrosis Factor-alpha (TNF-alpha)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks

Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Tumor Necrosis Factor-alpha (TNF-alpha) [units: Ratio] Median (Inter-Quartile Range)	1.0 (0.69 to 1.28)	1.0 (0.67 to 1.2)

37. Secondary Outcome Measure:

Measure Title	Serum Vascular Cell Adhesion Molecule-1 (VCAM-1)
Measure Description	Ratio of treatment period mean to run-in value
Time Frame	Baseline to 12 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS) was performed and was based on data from all subjects who were randomized, took at least 1 dose of study medication, and contributed sufficient data for calculation of this outcome Measure.

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Measured Values

	Symbicort+Tiotropium	Placebo+Tiotropium
Number of Participants Analyzed	304	309
Serum Vascular Cell Adhesion Molecule-1 (VCAM-1) [units: Ratio] Median (Inter-Quartile Range)	0.96 (0.87 to 1.06)	0.99 (0.91 to 1.09)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Symbicort+Tiotropium	Symbicort Turbuhaler® (budesonide/formoterol) 320/9 mcg, one inhalation twice daily and Spiriva® (tiotropium) 18 mcg, one inhalation once daily
Placebo+Tiotropium	Spiriva® (tiotropium) 18 mcg, one inhalation once daily and placebo Turbuhaler one inhalation once daily

Serious Adverse Events

	Symbicort+Tiotropium	Placebo+Tiotropium
	Affected/At Risk (%)	Affected/At Risk (%)
Total	10/329 (3.04%)	16/330 (4.85%)
Cardiac disorders		
Acute Coronary Syndrome †	1/329 (0.3%)	0/330 (0%)
Atrioventricular Block Second Degree †	0/329 (0%)	1/330 (0.3%)
Infections and infestations		
Infective Exacerbation of Chronic Obstructive Airways Disease †	2/329 (0.61%)	2/330 (0.61%)
Pneomonia †	1/329 (0.3%)	1/330 (0.3%)
Injury, poisoning and procedural complications		

	Symbicort+Tiotropium	Placebo+Tiotropium
	Affected/At Risk (%)	Affected/At Risk (%)
Pelvic Fracture †	0/329 (0%)	1/330 (0.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenocarcinoma Pancreas †	0/329 (0%)	1/330 (0.3%)
Lung Neoplasm †	1/329 (0.3%)	0/330 (0%)
Lung Neoplasm Malignant †	1/329 (0.3%)	0/330 (0%)
Respiratory, thoracic and mediastinal disorders		
Bronchospasm †	0/329 (0%)	1/330 (0.3%)
Chronic Obstructive Pulmonary Disease †	3/329 (0.91%)	8/330 (2.42%)
Haemoptysis †	0/329 (0%)	1/330 (0.3%)
Pleuritic Pain †	1/329 (0.3%)	0/330 (0%)

† Indicates events were collected by systematic assessment.

Other Adverse Events

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

	Symbicort+Tiotropium	Placebo+Tiotropium
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/329 (0%)	0/330 (0%)

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.

Prior to any publication or disclosure, the PI provides AstraZeneca with preliminary data and drafts and with the proposed final manuscript. AstraZeneca shall have a period of 30 days from receipt of the proposed final manuscript to review it and may within such time frame require that submission for publication or disclosure be delayed.

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