Clinical trial results:
A RANDOMISED, DOUBLE-BLIND, DOUBLE-DUMMY, ACTIVE-CONTROLLED STUDY EVALUATING THE EFFICACY, SAFETY AND TOLERABILITY OF TWICE-DAILY ACLIDINIUM BROMIDE/FORMOTEROL FUMARATE COMPARED WITH TWICE-DAILY SALMETEROL/FLUTICASONE PROPIONATE FOR 24-WEEKS TREATMENT IN SYMPTOMATIC PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Summary

EudraCT number	2013-000116-14
Trial protocol	HU GB IT LT CZ AT ES NL BG
Global end of trial date	04 August 2014

Results information

Result version number	v1 (current)
This version publication date	21 May 2016
First version publication date	21 May 2016

Trial information

Trial identification

Sponsor protocol code	M-40464-39

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01908140
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Avenida Diagonal 615, 2nd Floor, Barcelona, Spain, 08028
Public contact	Senior Director, Clinical Development, AstraZeneca, esther.garciagil@astrazeneca.com
Scientific contact	Study Information Center, AstraZeneca Barcelona, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 August 2014
Global end of trial reached?	Yes
Global end of trial date	04 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to compare the efficacy, safety and tolerability of aclidinium bromide/formoterol fumarate 400 µg/12 µg and salmeterol/fluticasone propionate 50/500 µg in patients with chronic obstructive pulmonary disease (COPD)

Protection of trial subjects:

This study was performed according to the regulations of each country where it was carried out, the directives of the Declaration of Helsinki for biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki (1964), revised at Tokyo (1975), Venice (1983), Hong Kong (1989), Somerset West (1996) and Edinburgh (2000) including the Notes of clarification made by the World Medical Assembly (WMA) of Washington (2002) and Tokyo (2004), and the 59th WMA General Assembly, Seoul (2008), as well as in compliance with the guidelines of the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines and local regulations

Every patient was provided with sufficient salbutamol for inhalation (pMDI 100µg/puff) to be used as relief medication during the study. Administration was on as needed basis, as per the investigator's instructions in accordance with the clinical status of the patient

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 47
Country: Number of subjects enrolled	Bulgaria: 62
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	Czech Republic: 25
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 254
Country: Number of subjects enrolled	Hungary: 98
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Lithuania: 27
Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Poland: 122
Country: Number of subjects enrolled	South Africa: 134
Country: Number of subjects enrolled	Spain: 62
Country: Number of subjects enrolled	United Kingdom: 37

Worldwide total number of subjects	933
EEA total number of subjects	781

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	550
From 65 to 84 years	382
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 140 activated sites. A total of 121 sites randomised patients. The first patient was screened in Oct 2013 and the last patient visit was in Aug 2014.

Pre-assignment

Screening details:

Patients fulfilling inclusion/exclusion criteria at the time of the screening visit were entered into a run-in period of 14-21 days to assess disease stability.

Pre-assignment period milestones

Number of subjects started	933
Number of subjects completed	933

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Aclidinium Bromide / Formoterol Fumarate

Arm description:

Aclidinium Bromide 400 µg / Formoterol Fumarate 12 µg BID for 24 Weeks

Arm type	Experimental
Investigational medicinal product name	Aclidinium Bromide / Formoterol Fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

400µg/12µg BID

Arm title	Salmeterol / Fluticasone

Arm description:

Salmeterol 50 µg / Fluticasone propionate 500 µg BID for 24 Weeks

Arm type	Active comparator
Investigational medicinal product name	Salmeterol / Fluticasone propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

50µg/500µg BID

Number of subjects in period 1	Aclidinium Bromide / Formoterol Fumarate	Salmeterol / Fluticasone
Started	468	465
Completed	402	386
Not completed	66	79
Consent withdrawn by subject	23	24
Adverse event, non-fatal	22	23
Lost to follow-up	1	6
Other or Progressive Disease	5	12
Lack of efficacy	7	5
Protocol deviation	8	9

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	933	933	
Age categorical Units: Subjects			
Adults (18-64 years)	550	550	
From 65-84 years	382	382	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	63.4		
standard deviation	± 7.8	-	
Gender, Male/Female Units: participants			
Female	326	326	
Male	607	607	

End points

End points reporting groups	
Reporting group title	Aclidinium Bromide / Formoterol Fumarate
Reporting group description:	
Aclidinium Bromide 400 µg / Formoterol Fumarate 12 µg BID for 24 Weeks	
Reporting group title	Salmeterol / Fluticasone
Reporting group description:	
Salmeterol 50 µg / Fluticasone propionate 500 µg BID for 24 Weeks	
Subject analysis set title	Aclidinium Bromide / Formoterol Fumarate
Subject analysis set type	Per protocol
Subject analysis set description:	
Aclidinium Bromide 400 µg / Formoterol Fumarate 12 µg BID for 24 Weeks	
Subject analysis set title	Salmeterol / Fluticasone
Subject analysis set type	Per protocol
Subject analysis set description:	
Salmeterol 50 µg / Fluticasone propionate 500 µg BID for 24 Weeks	

Primary: Peak forced expiratory volume in one second (FEV1) at week 24	
End point title	Peak forced expiratory volume in one second (FEV1) at week 24
End point description:	
Peak FEV1 define at the highest value observed in the 3h after the morning IMP administration	
End point type	Primary
End point timeframe:	
At Week 24	

End point values	Aclidinium Bromide / Formoterol Fumarate	Salmeterol / Fluticasone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	357	344		
Units: Liters				
least squares mean (standard error)	1.66 (± 0.011)	1.559 (± 0.011)		

Statistical analyses

Statistical analysis title	Peak FEV1 at week 24
Statistical analysis description:	
This sample size of 900 had 90% power to show that the lower bound of the two-sided 95% confidence interval for the difference between Aclidinium bromide 400 µg/Formoterol Fumarate 12 µg and SeretideTM AccuhalerTM (50/500 µg) in Peak FEV1 at 24 weeks is above -0.055 L	
Comparison groups	Aclidinium Bromide / Formoterol Fumarate v Salmeterol / Fluticasone

Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	MMRM
Parameter estimate	Least squares mean difference
Point estimate	0.101
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.131
Variability estimate	Standard deviation

Notes:

[1] - non-inferiority margin=-0.055 L

Secondary: Transition Dyspnoea Index (TDI) focal score at week 24

End point title	Transition Dyspnoea Index (TDI) focal score at week 24

End point description:

The TDI includes the same 3 categories as BDI and 7 ratings indicating the magnitude of the change from baseline in each category: from -3 (“major deterioration”) to zero (“no change”) to +3 (“major improvement”). Category scores are added to compute the Focal Score (from -9 to 9)

End point type	Secondary

End point timeframe:

Week 24

End point values	Aclidinium Bromide / Formoterol Fumarate	Salmeterol / Fluticasone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	353	341		
Units: TDI Focal Score				
least squares mean (standard error)	1.877 (± 0.171)	1.878 (± 0.173)		

Statistical analyses

Statistical analysis title	TDI focal score at week 24

Statistical analysis description:

The total sample size provided 81% nominal power to show that the lower bound of the two-sided 95 confidence interval for the difference between Aclidinium bromide 400 µg/Formoterol fumarate 12 µg and SeretideTM AccuhalerTM (50/500 µg) in transitional dyspnoea index (TDI) at 24 weeks is above -0.5

Comparison groups	Aclidinium Bromide / Formoterol Fumarate v Salmeterol / Fluticasone

Number of subjects included in analysis	694
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	> 0.05
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.461
upper limit	0.459

Notes:

[2] - non-inferiority limit -0.5 units

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
24 Weeks treatment + 2 weeks follow-up (±3 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Aclidinium Bromide / Formoterol Fumarate
Reporting group description:	
Aclidinium Bromide 400 µg / Formoterol Fumarate 12 µg BID for 24 Weeks	
Reporting group title	Salmeterol / Fluticasone
Reporting group description:	
Salmeterol 50 µg / Fluticasone propionate 500 µg BID for 24 Weeks	

Serious adverse events	Aclidinium Bromide / Formoterol Fumarate	Salmeterol / Fluticasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 467 (7.49%)	33 / 466 (7.08%)	
number of deaths (all causes)	3	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of head			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			

subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 467 (0.00%)	2 / 466 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chest Pain			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adnexa uteri mass			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
COPD (exacerbation)			
subjects affected / exposed	13 / 467 (2.78%)	8 / 466 (1.72%)	
occurrences causally related to treatment / all	0 / 15	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 467 (0.43%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizoaffective disorder depressive			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grastroenteritis radiation			

subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 467 (0.00%)	2 / 466 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arrhythmogenic right ventricular dysp			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Coronary Artery Disease			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial Infarction			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor Pulmonale			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Artrial fibrillation			
subjects affected / exposed	1 / 467 (0.21%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Artrial flutter			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 467 (0.21%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			

subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Gallbladder disorder			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Polymyalgia rheumatica			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			

subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Endometritis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 467 (0.43%)	4 / 466 (0.86%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 467 (0.21%)	0 / 466 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract and infection			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			

subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	0 / 467 (0.00%)	1 / 466 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Aclidinium Bromide / Formoterol Fumarate	Salmeterol / Fluticasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 467 (26.55%)	135 / 466 (28.97%)	
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 467 (6.00%)	32 / 466 (6.87%)	
occurrences (all)	42	46	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	70 / 467 (14.99%)	75 / 466 (16.09%)	
occurrences (all)	82	81	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	26 / 467 (5.57%)	28 / 466 (6.01%)	
occurrences (all)	30	33	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported