Clinical trial results:
Efficacy and safety of Symbicort® Turbuhaler® 160/4.5 g/inhalation, two inhalations twice daily plus as-needed, compared with Seretide™ Diskus™ 50/500 g/inhalation, one inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed - a 6-month, randomised, double-blind, parallel-group, active-controlled, multi-national phase IIIB study in adult and adolescent patients with persistent asthma (AHEAD)

Summary

EudraCT number	2004-004905-11
Trial protocol	DE ES
Global end of trial date	27 October 2006

Results information

Result version number	v1 (current)
This version publication date	28 April 2016
First version publication date	28 April 2016

Trial information

Trial identification

Sponsor protocol code	D5890C00002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	R&D Lund, SE-221 87 Lund, Sweden,
Public contact	Bjorn Rubin, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Bjorn Rubin, AstraZeneca, ClinicalTrialTransparency@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	27 October 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2006
Global end of trial reached?	Yes
Global end of trial date	27 October 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the efficacy of 2 inhalations of Symbicort Turbuhaler 160/4.5 µg/inhalation twice daily plus Symbicort Turbuhaler 160/4.5 µg/inhalation as-needed with 1 inhalation of Seretide Diskus 50/500 µg/inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed in patients with persistent asthma by evaluation of time to first severe asthma exacerbation as the primary outcome variable.

Protection of trial subjects:

The final clinical study protocol (CSP), including the final version of the Informed Consent Form, was approved or given a favourable opinion in writing by an Institutional Review Board (IRB) or Independent Ethics Committee (IEC). The investigator was to submit written approval to AstraZeneca before enrolling any patient into the study. In addition, before any participation in the genetic research part of the study took place, this part of the study (in CSP Appendix D) had to be approved by the appropriate IRB or IEC as well as the principal investigator(s).

The principal investigator at each centre was to ensure that the patients were given full and adequate oral and written information about the nature, purpose, possible risk, and possible benefit of the study. Patients were also to be notified that they were free to discontinue from the study at any time. The patients were to be given the opportunity to ask questions and allowed time to consider the information provided. For patients under age, this also applied to parent/legal guardian.

The patient's/parent's/legal guardian's signed and dated informed consent was to be obtained before conducting any procedure specifically for the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2005
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	Argentina: 383
Country: Number of subjects enrolled	Australia: 107
Country: Number of subjects enrolled	Brazil: 128
Country: Number of subjects enrolled	Canada: 135
Country: Number of subjects enrolled	China: 222
Country: Number of subjects enrolled	France: 139
Country: Number of subjects enrolled	Germany: 151
Country: Number of subjects enrolled	India: 40
Country: Number of subjects enrolled	Indonesia: 89

Country: Number of subjects enrolled	Malaysia: 57
Country: Number of subjects enrolled	Mexico: 224
Country: Number of subjects enrolled	Philippines: 62
Country: Number of subjects enrolled	Singapore: 15
Country: Number of subjects enrolled	South Africa: 392
Country: Number of subjects enrolled	Spain: 74
Country: Number of subjects enrolled	Thailand: 60
Country: Number of subjects enrolled	Vietnam: 31
Worldwide total number of subjects	2309
EEA total number of subjects	364

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)	324
Adults (18-64 years)	1822
From 65 to 84 years	163
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted in 17 countries between 2 May 2005 and 29 May 2006.

Pre-assignment

Screening details:

The study consisted of an enrolment visit, a 2-week run-in (standardization) period, randomization at Visit 2, and 3 further visits (Visits 3-5) at 4, 13 and 26 weeks. Subjects received 1 of 2 double-blinded treatments allocated in a random order.

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Symbicort SMART

Arm description:

Symbicort® Turbuhaler® 160/4.5 µg/inhalation,two inhalations twice daily plus as-needed

Arm type	Experimental
Investigational medicinal product name	Symbicort® Turbuhaler® 160/4.5 µg/inhalation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

2 inhalations twice daily

Arm title	Seretide

Arm description:

Seretide™ Diskus™ 50/500 µg/inhalation, one inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed

Arm type	Active comparator
Investigational medicinal product name	Seretide™ Diskus 50/500 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

1 inhalation twice daily

Number of subjects in period 1	Symbicort SMART	Seretide
Started	1154	1155
Completed	1056	1040
Not completed	98	115
Adverse event, non-fatal	11	20
Due to other reasons	38	46
Lost to follow-up	9	9
Protocol deviation	40	40

Baseline characteristics

Reporting groups	
Reporting group title	Symbicort SMART
Reporting group description:	
Symbicort® Turbuhaler® 160/4.5 µg/inhalation,two inhalations twice daily plus as-needed	
Reporting group title	Seretide
Reporting group description:	
Seretide™ Diskus™ 50/500 µg/inhalation, one inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed	

Reporting group values	Symbicort SMART	Seretide	Total
Number of subjects	1154	1155	2309
Age categorical			
Age			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	163	161	324
Adults (18-64 years)	910	912	1822
From 65-84 years	81	82	163
85 years and over	0	0	0
Age continuous			
Age			
Units: years			
arithmetic mean	39.6	39.2	
full range (min-max)	12 to 80	12 to 80	-
Gender categorical			
Units: Subjects			
Female	711	711	1422
Male	443	444	887

End points

End points reporting groups	
Reporting group title	Symbicort SMART
Reporting group description:	
Symbicort® Turbuhaler® 160/4.5 µg/inhalation,two inhalations twice daily plus as-needed	
Reporting group title	Seretide
Reporting group description:	
Seretide™ Diskus™ 50/500 µg/inhalation, one inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed	

Primary: Number of severe asthma exacerbations	
End point title	Number of severe asthma exacerbations
End point description:	
severe asthma exacerbations during the treatment period	
End point type	Primary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1151	1153		
Units: no. of patients with at least 1 event				
No of patients with at least one event	108	130		

Statistical analyses

Statistical analysis title	Time to first severe exacerbation
Statistical analysis description:	
Cox-proportional hazards model for time to first event	
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.05

Statistical analysis title	Number of severe asthma exacerbations
Statistical analysis description:	
Analysis of number of severe exacerbations reported per subject.	
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	Poisson Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.99

Secondary: Total daily no. of inhalations	
End point title	Total daily no. of inhalations
End point description:	
use of as-needed medication	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1143	1145		
Units: average daily no. of inhalations				
arithmetic mean (full range (min-max))	0.95 (0 to 7.6)	1.01 (0 to 8)		

Statistical analyses

Statistical analysis title	Total daily no. of inhalations
Statistical analysis description: Use of as-needed medication	
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2288
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.04

Secondary: Morning PEF(L/min)	
End point title	Morning PEF(L/min)
End point description:	
End point type	Secondary
End point timeframe: Morning	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1143	1145		
Units: L/min				
arithmetic mean (full range (min-max))	359.5 (134 to 702)	359.4 (119 to 735)		

Statistical analyses

Statistical analysis title	PEF (L/min)
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2288
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	2.8

Secondary: Evening PEF (L/min)

End point title	Evening PEF (L/min)
End point description:	
End point type	Secondary
End point timeframe:	
evening	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1143	1145		
Units: L/min				
arithmetic mean (full range (min-max))	362.3 (120 to 707)	361.7 (131 to 739)		

Statistical analyses

Statistical analysis title	Evening PEF
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2288
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	4.9

Secondary: Asthma symptoms - total score

End point title	Asthma symptoms - total score

End point description:

End point type	Secondary

End point timeframe:

26 weeks

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1140	1143		
Units: total score				
arithmetic mean (full range (min-max))	0.98 (0 to 5.2)	0.98 (0 to 5.2)		

Statistical analyses

Statistical analysis title	Asthma symptoms - total score
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.07

Secondary: Nights with awakenings due to asthma symptoms (%)

End point title	Nights with awakenings due to asthma symptoms (%)

End point description:

End point type	Secondary

End point timeframe:

26 weeks

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1140	1143		
Units: Percentage				
arithmetic mean (full range (min-max))	12 (0 to 100)	13.3 (0 to 100)		

Statistical analyses

Statistical analysis title	Nights with awakenings (%)
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	0.3

Secondary: Symptom free days (%)

End point title	Symptom free days (%)

End point description:

End point type	Secondary

End point timeframe:

26 weeks

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1144	1145		
Units: Percentage				
arithmetic mean (full range (min-max))	47.2 (0 to 100)	48.1 (0 to 100)		

Statistical analyses

Statistical analysis title	Symptom free days (%)
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.73
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	2.3

Secondary: Asthma control days (%)	
End point title	Asthma control days (%)
End point description:	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1144	1145		
Units: Percentage				
arithmetic mean (full range (min-max))	44 (0 to 100)	44.9 (0 to 100)		

Statistical analyses

Statistical analysis title	Asthma control days (%)
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	1.5

Secondary: Mild asthma exacerbations

End point title	Mild asthma exacerbations
End point description:	

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1144	1145		
Units: No. of patients with at least 1 event				
No of patients with at least one event	683	679		

Statistical analyses

Statistical analysis title	Time to first mild exacerbation
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.914
upper limit	1.131

Statistical analysis title	Number of mild exacerbations
Comparison groups	Symbicort SMART v Seretide

Number of subjects included in analysis	2289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.919
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.824
upper limit	1.024

Secondary: Mean FEV1 during the treatment period

End point title	Mean FEV1 during the treatment period
End point description:	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1135	1138		
Units: Litres				
arithmetic mean (full range (min-max))	2.522 (0.8 to 5.4)	2.494 (0.74 to 5.04)		

Statistical analyses

Statistical analysis title	Mean FEV1 during the treatment period
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2273
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.014

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.011
upper limit	0.039

Secondary: Asthma Control Questionnaire

End point title	Asthma Control Questionnaire
End point description:	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Symbicort SMART	Seretide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1105	1112		
Units: mean score				
arithmetic mean (full range (min-max))	1.08 (0 to 5)	1.12 (0 to 5.27)		

Statistical analyses

Statistical analysis title	ACQ
Comparison groups	Symbicort SMART v Seretide
Number of subjects included in analysis	2217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.59
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.071
upper limit	0.04

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the enrolment visit (visit 1) until visit 5 (26 weeks after randomisation). Only adverse events occuring after the start of randomised study medication are included in the summaries below.

Adverse event reporting additional description:

A total of 911 patients reported non-serious adverse events; 451 on Symbicort SMART, 460 on Seretide. Numbers for non-serious AEs in the reporting group table are based on the 5% threshold frequency.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Symbicort SMART

Reporting group description:

Symbicort® Turbuhaler® 160/4.5 µg/inhalation,two inhalations twice daily plus as-needed

Reporting group title	Seretide

Reporting group description:

Seretide™ Diskus™ 50/500 µg/inhalation, one inhalation twice daily plus terbutaline Turbuhaler 0.4 mg/inhalation as-needed

Serious adverse events	Symbicort SMART	Seretide	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 1151 (2.61%)	31 / 1153 (2.69%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events		0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign ovarian tumour			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma benign			

subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 1151 (0.09%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	5 / 1151 (0.43%)	5 / 1153 (0.43%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (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			
Wrist fracture			
subjects affected / exposed	1 / 1151 (0.09%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth fracture			

subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 1151 (0.00%)	2 / 1153 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 1151 (0.09%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 1151 (0.09%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson’s disease			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric polyps			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 1151 (0.00%)	2 / 1153 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bunion			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protusion			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 1151 (0.00%)	2 / 1153 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	2 / 1151 (0.17%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal abscess			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 1151 (0.09%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster ophthalmic			

subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis acute			
subjects affected / exposed	0 / 1151 (0.00%)	1 / 1153 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 1151 (0.17%)	2 / 1153 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 1151 (0.17%)	0 / 1153 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Symbicort SMART	Seretide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 1151 (9.64%)	111 / 1153 (9.63%)	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	64 / 1151 (5.56%)	61 / 1153 (5.29%)	
occurrences (all)	83	76	
Nasopharyngitis			
subjects affected / exposed	54 / 1151 (4.69%)	57 / 1153 (4.94%)	
occurrences (all)	67	63	

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