Clinical trial results:
A 6-week, phase III, double-blind, randomized, multi-centre, parallel-group study evaluating the efficacy and safety of 2 actuations Symbicort® (budesonide/formoterol) pMDI 40/2.25 g twice daily compared with 1 inhalation Symbicort® Turbuhaler® 80/4.5 g twice daily and 1 inhalation Pulmicort® (budesonide) Turbuhaler® 100 g twice daily in adult and adolescent asthmatics

Summary

EudraCT number	2007-002734-11
Trial protocol	HU CZ PL
Global end of trial date	21 July 2008

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	D5897C00003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	AstraZeneca R&D, SE-221 87 Lund, Sweden,
Public contact	Tomas Andersson, MD, AstraZeneca, aztrial_results_posting@astrazeneca.com
Scientific contact	Tomas Andersson, MD, AstraZeneca, aztrial_results_posting@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	21 July 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 July 2008
Global end of trial reached?	Yes
Global end of trial date	21 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to show that Symbicort pMDI 40/2.25 µg 2 actuations bid is more efficacious than Pulmicort Turbuhaler 100 µg 1 inhalation bid over a 6-week treatment period in adolescents and adults with asthma by evaluation of change in morning peak expiratory flow (PEF) from baseline to the treatment period as the primary outcome variable.

To compare the efficacy of Symbicort pMDI 40/2.25 µg 2 actuations bid with that of Symbicort Turbuhaler 80/4.5 µg 1 inhalation bid over a 6-week treatment period in adolescents and adults with asthma.

Protection of trial subjects:

The study was approved in 4 countries by the independent ethics committees in the respective country.

Informed consent was obtained from adult patients before any study specific procedure was conducted. For adolescent patients, informed consent was obtained from the patients' parents/legal guardians, and subjects signed the paediatric study subject assent form before any study specific procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2007
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	Poland: 264
Country: Number of subjects enrolled	Hungary: 227
Country: Number of subjects enrolled	Czech Republic: 132
Country: Number of subjects enrolled	Bulgaria: 119
Worldwide total number of subjects	742
EEA total number of subjects	742

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)	104
Adults (18-64 years)	591
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

898 subjects enrolled; 156 not randomised: 94 incorrect enrolment, 9 adverse events, 18 voluntary discontinuations, 1 lost to follow-up, 1use of not allowed medication, 1 non-compliant

Pre-assignment

Screening details:

The study consisted of an enrolment visit, a 2-week run-in (standardization) period, randomization at Visit 3, and 2 further visits (Visits 4, 5) at 3 and 6 weeks. Subjects received 1 of 3 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 pMDI

Arm description:

Symbicort®pMDI® 40/2.25 µg 2 Actuations Twice Daily

Arm type	Experimental
Investigational medicinal product name	Symbicort pMDI 40/2.25 µg 2 actuations bid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Symbicort pMDI 40/2.25 µg 2 actuations bid

Arm title	Symbicort Turbuhaler

Arm description:

Symbicort Turbuhaler® 80/4.5 µg 1 Inhalation Twice Daily

Arm type	Active comparator
Investigational medicinal product name	Symbicort Turbuhaler 80/4.5 µg 1 inhalation bid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Symbicort Turbuhaler 80/4.5 µg 1 inhalation bid

Arm title	Pulmicort Turbuhaler

Arm description:

Pulmicort®Turbuhaler® 100 µg 1 Inhalation Twice Daily

Arm type	Active comparator

Investigational medicinal product name	Pulmicort Turbuhaler 100 µg 1 inhalation bid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Pulmicort Turbuhaler 100 µg 1 inhalation bid

Number of subjects in period 1	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler
Started	253	246	243
Completed	249	241	238
Not completed	4	5	5
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	3	2	3
Other	1	1	-
Safety Reasons	-	-	1
Intake of prohibitted conmed	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Symbicort pMDI
Reporting group description:	
Symbicort®pMDI® 40/2.25 µg 2 Actuations Twice Daily	
Reporting group title	Symbicort Turbuhaler
Reporting group description:	
Symbicort Turbuhaler® 80/4.5 µg 1 Inhalation Twice Daily	
Reporting group title	Pulmicort Turbuhaler
Reporting group description:	
Pulmicort®Turbuhaler® 100 µg 1 Inhalation Twice Daily	

Reporting group values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler
Number of subjects	253	246	243
Age categorical 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)	33	34	37
Adults (18-64 years)	207	192	192
From 65-84 years	13	20	14
85 years and over	0	0	0
Age Continuous | Units: years			
arithmetic mean	41.2	41.4	39.3
full range (min-max)	12 to 75	12 to 76	12 to 78
Gender, Male/Female Units: Participants			
Female	152	142	131
Male	101	104	112
Race Units: Subjects			
White	253	246	243
Time since diagnosis Units: years			
median	7.1	6.5	7.8
full range (min-max)	1 to 44	1 to 56	1 to 40

Reporting group values	Total		
Number of subjects	742		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	104		
Adults (18-64 years)	591		
From 65-84 years	47		
85 years and over	0		
Age Continuous |			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender, Male/Female			
Units: Participants			
Female	425		
Male	317		
Race			
Units: Subjects			
White	742		
Time since diagnosis			
Units: years			
median			
full range (min-max)	-		

End points

End points reporting groups	
Reporting group title	Symbicort pMDI
Reporting group description: Symbicort®pMDI® 40/2.25 µg 2 Actuations Twice Daily	
Reporting group title	Symbicort Turbuhaler
Reporting group description: Symbicort Turbuhaler® 80/4.5 µg 1 Inhalation Twice Daily	
Reporting group title	Pulmicort Turbuhaler
Reporting group description: Pulmicort®Turbuhaler® 100 µg 1 Inhalation Twice Daily	

Primary: Morning Peak Expiratory Flow (PEF) (L/min)	
End point title	Morning Peak Expiratory Flow (PEF) (L/min)
End point description: Mean morning PEF on treatment (calculated as a mean using all available data after randomisation). No imputation of missing data was performed	
End point type	Primary
End point timeframe: Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Liters/min				
arithmetic mean (full range (min-max))	360 (145 to 797)	360 (190 to 673)	356 (147 to 623)	

Statistical analyses

Statistical analysis title	Change in mPEF (L/min)
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	8.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.26
upper limit	12.9

Statistical analysis title	Change in mPEF (L/min)
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.707
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.921
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.73
upper limit	3.88

Secondary: Evening Peak Expiratory Flow (PEF) (L/min)	
End point title	Evening Peak Expiratory Flow (PEF) (L/min)
End point description:	
Mean evening PEF on treatment (calculated as a mean using all available data after randomisation). No imputation of missing data was performed	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Liters/min				
arithmetic mean (full range (min-max))	372 (151 to 814)	370 (190 to 675)	366 (146 to 635)	

Statistical analyses

Statistical analysis title	change in ePEF (L/min)
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler

Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.11
upper limit	15.4

Statistical analysis title	Change in ePEF (L/min)
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.51
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.08
upper limit	6.18

Secondary: Asthma Symptom Score, Night

End point title	Asthma Symptom Score, Night

End point description:

Mean Asthma Symptom Score (Night) on treatment calculated as a mean using all available data after randomization, with run-in values as covariate). No imputation of missing data was performed. Daily scale:0 = No symptoms; 1 = Mild symptoms; 2 = Moderate symptoms; 3 = Severe symptoms.

End point type	Secondary

End point timeframe:

Baseline to 6 weeks

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Units on a scale				
arithmetic mean (full range (min-max))	0.878 (0 to 2.17)	0.852 (0 to 2.59)	0.98 (0 to 2.84)	

Statistical analyses

Statistical analysis title	Change in Asthma Symptom Score, Night
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.013
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.088
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.157
upper limit	-0.019

Statistical analysis title	Change in Asthma Symptom Score, Night
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.403
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.029
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.039
upper limit	0.098

Secondary: Asthma Symptom Score, Day

End point title	Asthma Symptom Score, Day

End point description:

Mean Asthma Symptom Score (Day) on treatment (calculated as a mean using all available data after randomization, with run-in values as covariate). No imputation of missing data was performed. Daily

scale:0 = No symptoms; 1 = Mild symptoms; 2 = Moderate symptoms; 3 = Severe symptoms

End point type	Secondary
End point timeframe: Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Units on a scale				
arithmetic mean (full range (min-max))	0.845 (0 to 2.74)	0.798 (0 to 2.54)	0.901 (0 to 2.87)	

Statistical analyses

Statistical analysis title	Change in Asthma Symptom Score, Day
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.075
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.127
upper limit	0.006

Statistical analysis title	Change in Asthma Symptom Score, day
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.347
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.032
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.035
upper limit	0.098

Secondary: Asthma Symptom Score, Total

End point title	Asthma Symptom Score, Total
End point description:	
Mean Asthma Symptom Score (Total) on treatment (calculated as a mean using all available data after randomization, with run-in values as covariate). No imputation of missing data was performed. Daily scale:0 = No symptoms; 1 = Mild symptoms; 2 = Moderate symptoms; 3 = Severe symptoms	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Units on a scale				
arithmetic mean (full range (min-max))	1.72 (0 to 4.91)	1.65 (0 to 5.13)	1.88 (0 to 5.72)	

Statistical analyses

Statistical analysis title	Change in Asthma Symptom Score, Total
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.023
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.148
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.275
upper limit	-0.02

Statistical analysis title	Change in Asthma Symptom Score, Total
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler

Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.356
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.067
upper limit	0.187

Secondary: Percentage of Nights With Awakenings Due to Asthma

End point title	Percentage of Nights With Awakenings Due to Asthma
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Percentage of night				
arithmetic mean (full range (min-max))	23.9 (0 to 100)	25.9 (0 to 100)	30.4 (0 to 100)	

Statistical analyses

Statistical analysis title	Percentage of Nights With Awakenings Due to Asthma
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-5.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.88
upper limit	-2.01

Statistical analysis title	Percentage of Nights With Awakenings Due to Asthma
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.743
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.655
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.58
upper limit	3.27

Secondary: Use of Rescue Medication, Night	
End point title	Use of Rescue Medication, Night
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Inhalations				
arithmetic mean (full range (min-max))	0.65 (0 to 4.74)	0.757 (0 to 8.17)	0.844 (0 to 5.66)	

Statistical analyses

Statistical analysis title	Use of Rescue Medication, Night
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler

Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.215
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	-0.1

Statistical analysis title	Use of Rescue Medication, Night
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.482
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.156
upper limit	0.074

Secondary: Use of Rescue Medication, Day	
End point title	Use of Rescue Medication, Day
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Inhalations				
arithmetic mean (full range (min-max))	0.289 (0 to 3.81)	0.329 (0 to 4.6)	0.407 (0 to 5.15)	

Statistical analyses

Statistical analysis title	Use of Rescue Medication, Day
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.013
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.165
upper limit	-0.02

Statistical analysis title	Use of Rescue Medication, Day
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.572
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.145
upper limit	0.052

Secondary: Use of Rescue Medication, Total	
End point title	Use of Rescue Medication, Total
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Inhalations				
arithmetic mean (full range (min-max))	0.939 (0 to 8.55)	1.09 (0 to 10.8)	1.25 (0 to 10.8)	

Statistical analyses

Statistical analysis title	Use of Rescue Medication, Total
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.303
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.473
upper limit	-0.132

Statistical analysis title	Use of Rescue Medication, Total
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.474
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.062
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.232
upper limit	0.108

Secondary: Percentage of Symptom-free Days

End point title	Percentage of Symptom-free Days
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Percentage of days				
arithmetic mean (full range (min-max))	18.9 (0 to 97.7)	22.4 (0 to 96.4)	15 (0 to 95.2)	

Statistical analyses

Statistical analysis title	Percentage of Symptom-free Days
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.126
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.891
upper limit	7.21

Statistical analysis title	Percentage of Symptom-free Days
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.186
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-2.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.77
upper limit	1.32

Secondary: Percentage of Asthma Control Days

End point title	Percentage of Asthma Control Days
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Percentage of days				
arithmetic mean (full range (min-max))	18.8 (0 to 97.7)	21.9 (0 to 96.4)	14.7 (0 to 95.2)	

Statistical analyses

Statistical analysis title	Percentage of Asthma Control Days
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.264
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.32
upper limit	1.73

Statistical analysis title	Percentage of Asthma Control Days
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler

Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.097
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	3.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.615
upper limit	7.45

Secondary: Percentage of Rescue free Days

End point title	Percentage of Rescue free Days
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	245	243	
Units: Percentage of days				
arithmetic mean (full range (min-max))	59 (0 to 100)	57.8 (0 to 100)	50.9 (0 to 100)	

Statistical analyses

Statistical analysis title	Percentage of Rescue free Days
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	7.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.18
upper limit	12.1

Statistical analysis title	Percentage of Rescue free Days
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.632
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.15
upper limit	3.73

Secondary: Forced Expiratory Volume in 1 Second (FEV1) (L)	
End point title	Forced Expiratory Volume in 1 Second (FEV1) (L)
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 6 weeks	

End point values	Symbicort pMDI	Symbicort Turbuhaler	Pulmicort Turbuhaler	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	243	242	
Units: Liters				
arithmetic mean (full range (min-max))	2.59 (0.855 to 5.69)	2.62 (1.18 to 4.86)	2.65 (0.88 to 4.92)	

Statistical analyses

Statistical analysis title	Change in FEV1 (L)
Comparison groups	Symbicort pMDI v Pulmicort Turbuhaler

Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.51
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0792
upper limit	0.0393

Statistical analysis title	Change in FEV1 (L)
Comparison groups	Symbicort pMDI v Symbicort Turbuhaler
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.096
Method	ANOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.0502
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.109
upper limit	0.00889

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the enrolment visit (visit 1) until visit 5 (6 weeks after randomisation). Only AEs occuring on or after the first dose of study medication are presented in the summaries below,

Adverse event reporting additional description:

A total of 99 patients reported non-serious adverse events; 38 on Symbicort pMDI, 30 on Symbicort Turbohaler, 31 on Pulmicort Turbohaler. Numbers for non-serious AEs in the reporting group table are based on the 2% threshold frequency.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Symbicort pMDI
Reporting group description: Symbicort pMDI	
Reporting group title	Pulmicort Turbuhaler
Reporting group description: Pulmicort Turbuhaler	
Reporting group title	Symbicort Turbuhaler
Reporting group description: Symbicort Turbuhaler	

Serious adverse events	Symbicort pMDI	Pulmicort Turbuhaler	Symbicort Turbuhaler
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 253 (0.00%)	1 / 243 (0.41%)	1 / 246 (0.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative dictionary used: MedDRA 10.1			
subjects affected / exposed	0 / 253 (0.00%)	1 / 243 (0.41%)	1 / 246 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Symbicort pMDI	Pulmicort Turbuhaler	Symbicort Turbuhaler
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 253 (8.30%)	14 / 243 (5.76%)	19 / 246 (7.72%)
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 253 (0.00%)	4 / 243 (1.65%)	2 / 246 (0.81%)
occurrences (all)	0	4	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 253 (2.37%)	4 / 243 (1.65%)	5 / 246 (2.03%)
occurrences (all)	6	4	5
Pharyngitis			
subjects affected / exposed	6 / 253 (2.37%)	3 / 243 (1.23%)	5 / 246 (2.03%)
occurrences (all)	6	3	5
Nasopharyngitis			
subjects affected / exposed	4 / 253 (1.58%)	2 / 243 (0.82%)	6 / 246 (2.44%)
occurrences (all)	4	2	6
Viral infection			
subjects affected / exposed	5 / 253 (1.98%)	3 / 243 (1.23%)	1 / 246 (0.41%)
occurrences (all)	5	3	1

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