Clinical trial results:
A randomized, multi-center, parallel group, double-blind, placebo and formoterol controlled 14 day dose ranging trial of 4 doses of indacaterol delivered via Twisthaler®, in adult and adolescent patients with persistent asthma

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2007-003191-19
Trial protocol	BE CZ ES HU GB PL SK DE
Global end of trial date	18 April 2008

Results information

Result version number	v2 (current)
This version publication date	08 July 2016
First version publication date	07 August 2015
Version creation reason	• Correction of full data set Corrected P-value in primary outcome measure for the comparison of Formoterol 12 µg v Indacaterol 500 µg

Trial information

Trial identification

Sponsor protocol code	CQMF149A2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00545272
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 April 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the dose response relationship among four doses of indacaterol treatment (62.5, 125, 250, and 500 micrograms [µg]) administered once daily (o.d.) and placebo as measured by the mean change from baseline to 24 hours (post-dose) trough forced expiratory volume (FEV1) after 14 days of treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Inhaled short acting β 2 -agonist (100 µg/ 90 µg salbutamol/albuterol) metered dose inhaler (MDI) or dry powder inhaler (DPI) formulation was allowed as rescue medication. Subjects were instructed to abstain from taking rescue salbutamol/ albuterol within the 6 hours of the start of each visit unless absolutely necessary. The investigator provided follow-up medical care for all subjects who were prematurely withdrawn from the study, or referred them for appropriate ongoing care.

Background therapy:

Subjects who were using a long acting β2-agonist (LABA) prior screening were moved to short acting β2-agonists (SABA) treatment as needed. Subjects who were using fixed-dose combinations, used inhaled corticosteroid monotherapy in addition to SABA as needed as background therapy in the study.

Evidence for comparator:

Formoterol fumarate, an approved medication for the treatment of subjects with asthma was used as an active comparator group in this study. Subjects were required to use inhaled corticosteroid at the standard recommended dose (12 µg twice daily) for the duration of the study.

Actual start date of recruitment	05 October 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: 82
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	Belgium: 61
Country: Number of subjects enrolled	Czech Republic: 56

Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Hungary: 40
Country: Number of subjects enrolled	South Africa: 35
Country: Number of subjects enrolled	Israel: 38
Worldwide total number of subjects	392
EEA total number of subjects	319

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)	25
Adults (18-64 years)	332
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 49 centres in 10 countries.

Pre-assignment

Screening details:

A total of 583 subjects were screened, of which 392 subjects were randomized into the study.

Period 1

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

Blinding implementation details:

The identity of the active and placebo treatments was concealed by the use of study drugs that were all identical in packaging, labeling, schedule of administration and appearance. A double-dummy design was used because the inhalers required for the administration of active comparator and experimental treatments were different. Unblinding was allowed in the case of subject emergencies, and at the conclusion of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Indacaterol 62.5 µg

Arm description:

Subjects received indacaterol 62.5 µg o.d., and placebo to formoterol twice daily (b.i.d.) for 14 days.

Arm type	Experimental
Investigational medicinal product name	Indacaterol
Investigational medicinal product code	QMF149
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Indacaterol 62.5 µg was delivered by the Twisthaler device o.d. for 14 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to formoterol was delivered by the Aerolizer device b.i.d. for 14 days.

Arm title	Indacaterol 125 µg

Arm description:

Subjects received indacaterol 125 µg o.d., and placebo to formoterol twice daily for 14 days.

Arm type	Experimental
Investigational medicinal product name	Indacaterol
Investigational medicinal product code	QMF149
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details: Indacaterol 125 µg was delivered by the Twisthaler device o.d. for 14 days	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details: Placebo to formoterol was delivered by the Aerolizer device twice daily for 14 days.	
Arm title	Indacaterol 250 µg
Arm description: Subjects received indacaterol 250 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Indacaterol
Investigational medicinal product code	QMF149
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details: Indacaterol 250 µg was delivered by the Twisthaler device o.d. for 14 days	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details: Placebo to formoterol was delivered by the Aerolizer device b.i.d. for 14 days.	
Arm title	Indacaterol 500 µg
Arm description: Subjects received indacaterol 500 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Indacaterol
Investigational medicinal product code	QMF149
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details: Indacaterol 500 µg was delivered by the Twisthaler device o.d. for 14 days	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use
Dosage and administration details: Placebo to formoterol was delivered by the Aerolizer device b.i.d. for 14 days.	
Arm title	Formoterol 12 µg
Arm description: Subjects received formoterol 12 µg b.i.d., and placebo to indacaterol o.d. for 14 days.	
Arm type	Active comparator

Investigational medicinal product name	Formoterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Formoterol 12 µg was delivered by the Aerolizer device b.i.d. for 14 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to indacaterol was delivered by the Twisthaler device o.d. for 14 days.

Arm title	Placebo

Arm description:

Subjects received placebo to indacaterol o.d., and placebo to formoterol twice daily for 14 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to indacaterol was delivered by the Twisthaler device o.d. for 14 days.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo to formoterol was delivered by the Aerolizer device b.i.d. for 14 days.

Number of subjects in period 1	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg
Started	61	68	65
Completed	61	67	64
Not completed	0	1	1
Adverse event, non-fatal	-	-	1
Abnormal laboratory value	-	-	-
Lost to follow-up	-	-	-
Abnormal test procedure result	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	Indacaterol 500 µg	Formoterol 12 µg	Placebo
Started	72	64	62

Completed	71	62	59
Not completed	1	2	3
Adverse event, non-fatal	-	-	1
Abnormal laboratory value	-	-	1
Lost to follow-up	-	1	-
Abnormal test procedure result	-	1	-
Protocol deviation	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Indacaterol 62.5 µg
Reporting group description:	
Subjects received indacaterol 62.5 µg o.d., and placebo to formoterol twice daily (b.i.d.) for 14 days.	
Reporting group title	Indacaterol 125 µg
Reporting group description:	
Subjects received indacaterol 125 µg o.d., and placebo to formoterol twice daily for 14 days.	
Reporting group title	Indacaterol 250 µg
Reporting group description:	
Subjects received indacaterol 250 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Reporting group title	Indacaterol 500 µg
Reporting group description:	
Subjects received indacaterol 500 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Reporting group title	Formoterol 12 µg
Reporting group description:	
Subjects received formoterol 12 µg b.i.d., and placebo to indacaterol o.d. for 14 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo to indacaterol o.d., and placebo to formoterol twice daily for 14 days.	

Reporting group values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg
Number of subjects	61	68	65
Age categorical Units: Subjects			
Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			
Age continuous Units: years arithmetic mean standard deviation	 41.3 ± 16.27	 38.4 ± 17.25	 36.6 ± 15.76
Gender categorical Units: Subjects			
Female Male	28 33	37 31	36 29

Reporting group values	Indacaterol 500 µg	Formoterol 12 µg	Placebo
Number of subjects	72	64	62
Age categorical Units: Subjects			
Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			
Age continuous Units: years arithmetic mean standard deviation	 40.1 ± 15.47	 44 ± 17.98	 39.8 ± 15.82

Gender categorical Units: Subjects			
Female	39	27	37
Male	33	37	25

Reporting group values	Total		
Number of subjects	392		
Age categorical Units: Subjects			
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	204		
Male	188		

End points

End points reporting groups

Reporting group title	Indacaterol 62.5 µg
Reporting group description:	
Subjects received indacaterol 62.5 µg o.d., and placebo to formoterol twice daily (b.i.d.) for 14 days.	
Reporting group title	Indacaterol 125 µg
Reporting group description:	
Subjects received indacaterol 125 µg o.d., and placebo to formoterol twice daily for 14 days.	
Reporting group title	Indacaterol 250 µg
Reporting group description:	
Subjects received indacaterol 250 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Reporting group title	Indacaterol 500 µg
Reporting group description:	
Subjects received indacaterol 500 µg o.d., and placebo to formoterol b.i.d. for 14 days.	
Reporting group title	Formoterol 12 µg
Reporting group description:	
Subjects received formoterol 12 µg b.i.d., and placebo to indacaterol o.d. for 14 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo to indacaterol o.d., and placebo to formoterol twice daily for 14 days.	

Primary: Change from baseline in trough forced expiratory volume in 1 second (FEV1) at Day 14

End point title	Change from baseline in trough forced expiratory volume in 1 second (FEV1) at Day 14

End point description:

The FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. Baseline FEV1 was defined as the average of two FEV1 assessments taken at 50 minutes and 15 minutes before the first study drug administration. Trough FEV1 was defined as the mean of 2 FEV1 measurements at 23 hour 10 minutes and 23 hours 45 minutes post-dose. If one of these assessments was missing then the trough was equal to the non-missing assessment. Positive change from baseline in trough favored experimental treatment. The analysis was performed in Intent to treat (ITT) population, defined as all randomized subjects who had a baseline and at least one post-dose measurement.

End point type	Primary

End point timeframe:

Day 1 Baseline (prior to first dose), Day 15 (24 hours after last dose)

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	67	63	68
Units: litres (L)				
least squares mean (standard error)	0.039 (± 0.0408)	0.054 (± 0.0383)	0.124 (± 0.0401)	0.166 (± 0.0381)

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: litres (L)				
least squares mean (standard error)	0.075 (± 0.0405)	-0.018 (± 0.0415)		

Statistical analyses

Statistical analysis title	Change in trough FEV1 (Indacaterol versus Placebo)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Placebo v Indacaterol 62.5 µg
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0298 [1]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.165
Variability estimate	Standard error of the mean
Dispersion value	0.0547

Notes:

[1] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol versus Placebo)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Placebo v Indacaterol 125 µg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176 [2]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.072

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.033
upper limit	0.177
Variability estimate	Standard error of the mean
Dispersion value	0.0533

Notes:

[2] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol versus Placebo)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Placebo v Indacaterol 250 µg
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [3]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.142
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.036
upper limit	0.248
Variability estimate	Standard error of the mean
Dispersion value	0.0541

Notes:

[3] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol versus Placebo)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Placebo v Indacaterol 500 µg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.184
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.289
Variability estimate	Standard error of the mean
Dispersion value	0.0531

Notes:

[4] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol versus Placebo)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Placebo v Formoterol 12 µg
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086 [5]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.093
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.013
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.0543

Notes:

[5] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol vs formoterol)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Indacaterol 62.5 µg v Formoterol 12 µg
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.499 [6]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.036
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.142
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.0539

Notes:

[6] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol vs formoterol)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Formoterol 12 µg v Indacaterol 125 µg
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.687 [7]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-0.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.124
upper limit	0.082
Variability estimate	Standard error of the mean
Dispersion value	0.0524

Notes:

[7] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol vs formoterol)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Formoterol 12 µg v Indacaterol 250 µg
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.362 [8]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.049
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.056
upper limit	0.153
Variability estimate	Standard error of the mean
Dispersion value	0.0532

Notes:

[8] - p-value was not adjusted for multiplicity.

Statistical analysis title	Change in trough FEV1 (Indacaterol vs formoterol)

Statistical analysis description:

Change from baseline to (24 hour post dose) trough FEV1 (L) was analyzed using Analysis of Covariance ANCOVA adjusting for treatment and region with baseline FEV1 as a covariate

Comparison groups	Formoterol 12 µg v Indacaterol 500 µg

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.082 [9]
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.091
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.012
upper limit	0.194
Variability estimate	Standard error of the mean
Dispersion value	0.0523

Notes:

[9] - p-value was not adjusted for multiplicity.

Secondary: Change from baseline in trough forced expiratory volume in 1 second (FEV1) at Day 1

End point title	Change from baseline in trough forced expiratory volume in 1 second (FEV1) at Day 1

End point description:

The FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. Baseline FEV1 was defined as the average of two FEV1 assessments taken at 50 minutes and 15 minutes before the first study drug administration. Trough FEV1 was defined as the mean of 2 FEV1 measurements at 23 hour 10 minutes and 23 hours 45 minutes post-dose. If one of these assessments was missing then the trough was equal to the non-missing assessment. Positive change from baseline in trough favored experimental treatment. The analysis was perfumed in ITT population.

End point type	Secondary

End point timeframe:

Day 1 baseline (prior to first-dose), Day 1 (24 hours post first-dose)

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	68	64	69
Units: Litres				
least squares mean (standard error)	0.054 (± 0.0347)	0.081 (± 0.0326)	0.143 (± 0.0339)	0.141 (± 0.0326)

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	62		
Units: Litres				
least squares mean (standard error)	0.155 (± 0.0341)	0.01 (± 0.0344)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Peak Forced Expiratory Volume in 1 Second (FEV1) on Day 1 and Day 14

End point title	Time to Peak Forced Expiratory Volume in 1 Second (FEV1) on Day 1 and Day 14

End point description:

FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. Time to peak FEV1 was calculated in minutes from the time of inhalation of study drug to the time of the peak FEV1, which is taken as the maximum FEV1 recorded post-dose. The analysis was performed in the ITT population.

End point type	Secondary

End point timeframe:

Day 1 and Day 14 (pre-dose and up to 4 hours post-dose)

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	68	65	72
Units: minutes				
arithmetic mean (standard deviation)				
Day 1 (n= 61, 68, 65, 71, 64, 62)	91 (± 83.02)	109.6 (± 81.09)	119 (± 81.64)	116.2 (± 75.5)
Day 14 (n=61, 66, 64, 70, 62, 59)	103.8 (± 86.67)	118.7 (± 88.42)	96.7 (± 70.65)	114 (± 76.41)

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	62		
Units: minutes				
arithmetic mean (standard deviation)				
Day 1 (n= 61, 68, 65, 71, 64, 62)	105.6 (± 70.64)	90.5 (± 82.46)		
Day 14 (n=61, 66, 64, 70, 62, 59)	114.6 (± 71.64)	80.4 (± 76.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume in 1 Second (FEV1) area under the curve from baseline to 4 hours post-dose (AUC 0-4) on Day 1 and Day 14

End point title	Forced Expiratory Volume in 1 Second (FEV1) area under the curve from baseline to 4 hours post-dose (AUC 0-4) on Day 1 and Day 14

End point description:

FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. FEV1 AUC (0-4) was evaluated for subjects with complete or incomplete FEV1 assessments, based on the observed FEV1 measurements. The missing FEV1 measurements were not interpolated. The analyses was performed in ITT population and accounted all subjects with at least one FEV1 assessment between baseline (pre-dose) and 4 hours post-dose. Here 'n' signifies those subjects evaluable for the outcome measure, at specified time-points, respectively.

End point type	Secondary

End point timeframe:

Day 1 and Day 14 (pre-dose, 5, 20 and 30 minutes, 1, 2, 3, and 4 hours post-dose)

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	68	65	72
Units: Litres				
least squares mean (standard error)				
Day 1 (n=61, 68, 65, 71, 64, 62)	2.668 (± 0.0281)	2.687 (± 0.0264)	2.726 (± 0.0272)	2.753 (± 0.0259)
Day 14 (n=61, 66, 64, 69, 62, 59)	2.67 (± 0.0419)	2.698 (± 0.04)	2.772 (± 0.0411)	2.786 (± 0.0393)

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	62		
Units: Litres				
least squares mean (standard error)				
Day 1 (n=61, 68, 65, 71, 64, 62)	2.832 (± 0.0274)	2.547 (± 0.0279)		
Day 14 (n=61, 66, 64, 69, 62, 59)	2.821 (± 0.0418)	2.565 (± 0.0426)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morning and Evening Peak Expiratory Flow at Day 14

End point title	Change From Baseline in Morning and Evening Peak Expiratory Flow at Day 14

End point description:

The Peak Expiratory Flow (PEF) is a convenient for monitoring of airway function at home, and it is commonly used to assess response to treatment or to document diurnal variation. PEF rate is the maximal rate that a person can exhale during a short maximal expiratory effort after fully inhaling. The PEF was measured using a peak flow meter every morning and evening during the study, prior administration of study medication, except evenings on the day of clinic visits. Change from baseline was the difference between the mean baseline PEF recorded during the screening period until the first day of treatment, and the overall mean PEF from Day 1 to 14. The analysis was performed in ITT population. Here 'n' signifies those subjects evaluable for this measure at specified time-points, respectively.

End point type	Secondary

End point timeframe:

Baseline (screening period), Day 1 up to Day 14 (treatment period)

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	68	65	72
Units: Litres/minute				
arithmetic mean (standard deviation)				
Morning PEF (n=56, 61, 53, 63, 57, 48)	18.7 (± 29.28)	17.2 (± 34.07)	25.7 (± 38.37)	25.8 (± 47.36)
Evening PEF (n=56, 58, 54, 59, 55, 47)	5.9 (± 36.92)	4.2 (± 37.82)	18.4 (± 36.7)	25.8 (± 38.07)

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	62		
Units: Litres/minute				
arithmetic mean (standard deviation)				
Morning PEF (n=56, 61, 53, 63, 57, 48)	25.2 (± 38.28)	-4.3 (± 43)		
Evening PEF (n=56, 58, 54, 59, 55, 47)	26.2 (± 35.01)	-11.4 (± 50.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects using rescue medication during day and night

End point title	Number of subjects using rescue medication during day and night

End point description:

Subjects recorded the use of rescue medications (salbutamol/albuterol) for treatment of asthma symptoms in a diary during day and night. Rescue medication during the day time was defined as number of puffs of rescue medication used in the 6 hours prior to evening PEF measurement. Rescue medication during the night time was defined as number of puffs of rescue medication used in the 12 hours prior recording the morning PEF measurement. The analysis was performed in ITT population.

End point type	Secondary

End point timeframe:
Day 1 up to Day 14

End point values	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg	Indacaterol 500 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	68	65	72
Units: Subjects				
number (not applicable)				
Day	33	43	28	35
Night	36	40	36	34

End point values	Formoterol 12 µg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	62		
Units: Subjects				
number (not applicable)				
Day	30	39		
Night	31	40		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	Indacaterol 62.5 µg
Reporting group description: Indacaterol 62.5 µg	
Reporting group title	Indacaterol 125 µg
Reporting group description: Indacaterol 125 µg	
Reporting group title	Indacaterol 250 µg
Reporting group description: Indacaterol 250 µg	
Reporting group title	Indacaterol 500 µg
Reporting group description: Indacaterol 500 µg	
Reporting group title	Formoterol 12 µg
Reporting group description: Formoterol 12 µg	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)	0 / 68 (0.00%)	0 / 65 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 68 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Indacaterol 500 µg	Formoterol 12 µg	Placebo
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 72 (0.00%)	0 / 64 (0.00%)	1 / 62 (1.61%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 64 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 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	Indacaterol 62.5 µg	Indacaterol 125 µg	Indacaterol 250 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 61 (6.56%)	6 / 68 (8.82%)	8 / 65 (12.31%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 68 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 61 (3.28%)	1 / 68 (1.47%)	2 / 65 (3.08%)
occurrences (all)	2	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 61 (3.28%)	2 / 68 (2.94%)	4 / 65 (6.15%)
occurrences (all)	2	2	4
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 61 (0.00%)	2 / 68 (2.94%)	0 / 65 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 68 (1.47%)	2 / 65 (3.08%)
occurrences (all)	0	1	2

Non-serious adverse events	Indacaterol 500 µg	Formoterol 12 µg	Placebo
Total subjects affected by non-serious adverse events			

subjects affected / exposed	14 / 72 (19.44%)	3 / 64 (4.69%)	3 / 62 (4.84%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 72 (2.78%)	0 / 64 (0.00%)	0 / 62 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	2 / 72 (2.78%)	2 / 64 (3.13%)	2 / 62 (3.23%)
occurrences (all)	2	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 72 (11.11%)	0 / 64 (0.00%)	1 / 62 (1.61%)
occurrences (all)	8	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 72 (1.39%)	0 / 64 (0.00%)	0 / 62 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 72 (1.39%)	1 / 64 (1.56%)	0 / 62 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2007	The protocol was amended for compliance with national regulations or clinical practice concerning the inclusion of subjects less than 18 years of age in clinical trials and time frame for collection of AEs was modified to start after administration of first dose of study treatments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported