Clinical trial results:
A Comparative Study of Inhaled Ciclesonide Versus Placebo in Children with Asthma (RAINBOW)

Summary

EudraCT number	2006-000803-40
Trial protocol	DE ES HU
Global end of trial date	17 August 2007

Results information

Result version number	v1 (current)
This version publication date	22 July 2016
First version publication date	22 July 2016

Trial information

Trial identification

Sponsor protocol code	BY9010/M1-209

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00384189
WHO universal trial number (UTN)	U1111-1172-2297

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	One Takeda Parkway, Deerfield , IL, United States,
Public contact	Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosures@takeda.com
Scientific contact	Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosures@takeda.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?	Yes
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	17 August 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 August 2007
Global end of trial reached?	Yes
Global end of trial date	17 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to investigate the efficacy of inhaled ciclesonide at three different dose levels compared with placebo with respect to pulmonary function, asthma symptoms, and use of rescue medication in children aged 6-11 years with asthma. Treatment medication will be administered as follows: ciclesonide or placebo will be inhaled once daily in the evening. The study consists of a baseline period (2 to 4 weeks) and a treatment period (12 weeks). The study provides further data on safety and tolerability of ciclesonide.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 September 2006
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	Bulgaria: 112
Country: Number of subjects enrolled	Germany: 53
Country: Number of subjects enrolled	Hungary: 152
Country: Number of subjects enrolled	Poland: 170
Country: Number of subjects enrolled	Romania: 60
Country: Number of subjects enrolled	Russian Federation: 189
Country: Number of subjects enrolled	South Africa: 112
Country: Number of subjects enrolled	Spain: 62
Country: Number of subjects enrolled	Ukraine: 170
Worldwide total number of subjects	1080
EEA total number of subjects	609

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)	1080
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 110 investigative sites in Bulgaria, Germany, Hungary, Poland, Romania, Russia, South Africa, Spain, and Ukraine from 29 September 2006 to 17 August 2007.

Pre-assignment

Screening details:

Children with a diagnosis of asthma were enrolled equally in 1 of 4 treatment groups, once a day placebo, 40 µg, 80 µg or 160 µg ciclesonide.

Period 1

Period 1 title	Randomized
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Ciclesonide 40 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with 1,1,1,2-hydrofluoroalkane (HFA)-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator
Investigational medicinal product name	Placebo-matching ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Ciclesonide 80 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening

for 2 to 4 weeks in the Baseline period followed by ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Ciclesonide 160 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder

Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Placebo

Arm description:

Placebo-matching Ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Number of subjects in period 1	Ciclesonide 40 µg	Ciclesonide 80 µg	Ciclesonide 160 µg
Started	305	312	313
Completed	304	312	311
Not completed	1	0	2
Did Not Receive Treatment	1	-	2

Number of subjects in period 1	Placebo
Started	150
Completed	146
Not completed	4
Did Not Receive Treatment	4

Period 2

Period 2 title	Randomized, Actual Treatment Received
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Ciclesonide 40 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Ciclesonide 80 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Ciclesonide 160 µg

Arm description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm title	Placebo

Arm description:

Placebo-matching Ciclesonide ,inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period.

Investigational medicinal product name	Ciclesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

Ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks.

Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Seven participants in Period 1 were randomized but not treated. Baseline characteristics for these 7 participants are not being reported.

Number of subjects in period 2[2]	Ciclesonide 40 µg	Ciclesonide 80 µg	Ciclesonide 160 µg
Started	305	312	310
Completed	255	255	255
Not completed	50	57	55
Other Reason Not Specified	50	57	55

Number of subjects in period 2[2]	Placebo
Started	146
Completed	110
Not completed	36
Other Reason Not Specified	36

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Seven participants were randomized but did not receive treatment. These 7 participants are included in the worldwide number enrolled because they were randomized but baseline characteristics are not being reported for them.

Baseline characteristics

Reporting groups	
Reporting group title	Ciclesonide 40 µg
Reporting group description:	
Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.	
Reporting group title	Ciclesonide 80 µg
Reporting group description:	
Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.	
Reporting group title	Ciclesonide 160 µg
Reporting group description:	
Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.	
Reporting group title	Placebo
Reporting group description:	
Placebo-matching Ciclesonide ,inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.	

Reporting group values	Ciclesonide 40 µg	Ciclesonide 80 µg	Ciclesonide 160 µg
Number of subjects	305	312	310
Age categorical Units: Subjects			
Children (2-11 years)	305	312	310
Age Continuous Units: years			
arithmetic mean	8.4	8.4	8.7
standard deviation	± 1.7	± 1.6	± 1.6
Gender, Male/Female Units: participants			
Female	95	121	92
Male	210	191	218
Race/Ethnicity, Customized Units: Subjects			
Caucasian	276	279	277
Non-Caucasian	29	33	33
Region of Enrollment Units: Subjects			
Bulgaria	29	33	33
Germany	17	16	12
Hungary	42	45	43
Poland	49	48	49
Romania	15	16	21

Russian Federation	54	52	55
South Africa	32	34	32
Spain	18	18	17
Ukraine	49	50	48
Inhaled Glucocorticosteroids (ICS) Pretreatment Units: Subjects			
Yes	200	204	199
No	105	108	111
Asthma Severity According to Global Initiative for Asthma (GINA) Units: Subjects			
Intermittent	20	19	13
Mild	25	22	29
Moderate	112	110	104
Severe	148	161	164
Height Units: cm			
arithmetic mean	134.6	134.5	135.9
standard deviation	± 10.8	± 11	± 10.8
Weight Units: kg			
arithmetic mean	32.3	31.9	33.2
standard deviation	± 9.1	± 9.3	± 9.5
Duration of Asthma Units: months			
arithmetic mean	44.3	45.5	45.5
standard deviation	± 27.7	± 27.8	± 27.4
Inhaled glucocorticosteroids (ICS) Pretreatment Dose			
The number of participants who received ICS pretreatment is 200, 204, 199 and 102 in each treatment arm, respectively.			
Units: µg/day			
arithmetic mean	211.9	228.8	205
standard deviation	± 181.9	± 188.8	± 177.1

Reporting group values	Placebo	Total	
Number of subjects	146	1073	
Age categorical Units: Subjects			
Children (2-11 years)	146	1073	
Age Continuous Units: years			
arithmetic mean	8.4		
standard deviation	± 1.7	-	
Gender, Male/Female Units: participants			
Female	54	362	
Male	92	711	
Race/Ethnicity, Customized Units: Subjects			
Caucasian	133	965	

Non-Caucasian	13	108	
Region of Enrollment Units: Subjects			
Bulgaria	15	110	
Germany	8	53	
Hungary	22	152	
Poland	23	169	
Romania	8	60	
Russian Federation	27	188	
South Africa	13	111	
Spain	8	61	
Ukraine	22	169	
Inhaled Glucocorticosteroids (ICS) Pretreatment Units: Subjects			
Yes	102	705	
No	44	368	
Asthma Severity According to Global Initiative for Asthma (GINA) Units: Subjects			
Intermittent	7	59	
Mild	10	86	
Moderate	50	376	
Severe	79	552	
Height Units: cm			
arithmetic mean	134.6		
standard deviation	± 11.1	-	
Weight Units: kg			
arithmetic mean	32.7		
standard deviation	± 9.7	-	
Duration of Asthma Units: months			
arithmetic mean	47.6		
standard deviation	± 28	-	
Inhaled glucocorticosteroids (ICS) Pretreatment Dose			
The number of participants who received ICS pretreatment is 200, 204, 199 and 102 in each treatment arm, respectively.			
Units: µg/day			
arithmetic mean	224.6		
standard deviation	± 178.8	-	

End points

End points reporting groups

Reporting group title	Ciclesonide 40 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with 1,1,1,2-hydrofluoroalkane (HFA)-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 80 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 160 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Placebo

Reporting group description:

Placebo-matching Ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 40 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI) with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 80 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 80 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 160 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Placebo

Reporting group description:

Placebo-matching Ciclesonide ,inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI with HFA-134a as propellant, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Subject analysis set title	Ciclesonide 40 µg Intent-to-Treat (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants randomized to the Ciclesonide 40 µg who received at least one dose of study, regardless of dose, with data available for analysis.

Subject analysis set title	Ciclesonide 80 µg ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants randomized to the Ciclesonide 80 µg who received at least one dose of study, regardless of dose, with data available for analysis.

Subject analysis set title	Ciclesonide 160 µg ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants randomized to the Ciclesonide 160 µg who received at least one dose of study, regardless of dose, with data available for analysis.

Subject analysis set title	Placebo ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants randomized to Placebo who received at least one dose of study, regardless of dose, with data available for analysis.

Primary: Change from Baseline in Morning Peak Expiratory Flow (PEF)

End point title	Change from Baseline in Morning Peak Expiratory Flow (PEF)

End point description:

PEF is the maximum speed of expiration. A portable electronic PEF meter was used for the home PEF readings. The patients recorded PEF daily, in the morning immediately after getting up. Readings were done preferably at least 4 hours after use of rescue medication and before inhalation of the study medication. At each measurement, three readings were obtained in the standing position. All three values were recorded in the diary; the highest value was used for evaluation. The higher change from Baseline values are the best. Analysis of covariance (ANCOVA) model with the baseline value and age as covariates was used for analysis. Last observation carried forward.

End point type	Primary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304	312	311	146
Units: liters/minute				
least squares mean (standard error)	15.23 (± 2.69)	14.79 (± 2.6)	17.37 (± 2.68)	5.4 (± 3.71)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ciclesonide 40 µg Intent-to-Treat (ITT) v Placebo ITT
Number of subjects included in analysis	450
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0116 [1]
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	9.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	18.3
Variability estimate	Standard error of the mean
Dispersion value	4.3

Notes:

[1] - Baseline value and age as covariates. One-sided p-value, significance level 2.5%.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Ciclesonide 80 µg ITT v Placebo ITT
Number of subjects included in analysis	458
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0148 [2]
Method	ANCOVA
Parameter estimate	Least Square Means Difference
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	17.8
Variability estimate	Standard error of the mean
Dispersion value	4.3

Notes:

[2] - Baseline value and age as covariates. One-sided p-value, significance level 2.5%.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Ciclesonide 160 µg ITT v Placebo ITT
Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0028 [3]
Method	ANCOVA
Parameter estimate	Least Squares Means Difference
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	20.4
Variability estimate	Standard error of the mean
Dispersion value	4.3

Notes:

[3] - Baseline value and age as covariates. One-sided p-value, significance level 2.5%.

Secondary: Time to First Event of Lack of Efficacy (LOE) by Week 12	
End point title	Time to First Event of Lack of Efficacy (LOE) by Week 12

End point description:

Kaplan Meier Estimates of the probability of not experiencing LOE by Week 12 was measured. LOE was reached if any of the following criteria occurred during the treatment period: • asthma exacerbation (a worsening of asthma symptoms requiring a change in medication; • nocturnal awakenings due to asthma on any 4 or more nights during any 7-consecutive-day period; • use of more than 8 puffs/day of salbutamol on any 4 or more days during any 7-consecutive-day period; • decrease in morning PEF to <80% of randomization value on any 4 consecutive days during the treatment period.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304	312	311	146
Units: Percent				
number (not applicable)	72.8	74.5	73.2	66.9

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ciclesonide 40 µg Intent-to-Treat (ITT) v Placebo ITT
Number of subjects included in analysis	450
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1362 [4]
Method	Logrank

Notes:

[4] - Two-sided p-value, significance level 5%.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Ciclesonide 80 µg ITT v Placebo ITT
Number of subjects included in analysis	458
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0891 [5]
Method	Logrank

Notes:

[5] - Two-sided p-value, significance level 5%.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Ciclesonide 160 µg ITT v Placebo ITT

Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1574 [6]
Method	Logrank

Notes:

[6] - Two-sided p-value, significance level 5%.

Secondary: Percentage of Days with Asthma Control Based on Symptoms, Use of Rescue Medication, Morning PEF and PEF Fluctuation

End point title	Percentage of Days with Asthma Control Based on Symptoms, Use of Rescue Medication, Morning PEF and PEF Fluctuation

End point description:

Control of asthma was evaluated on a daily basis (24 hours) using the following variables: asthma symptoms, use of rescue medication, morning (am) PEF and PEF fluctuation. The median percentage of days with asthma control is presented.

End point type	Secondary

End point timeframe:

28 days prior to last visit (Up to 12 Weeks)

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	302	311	309	144
Units: percentage of days				
median (full range (min-max))	7.14 (0 to 100)	10.53 (0 to 100)	6.67 (0 to 100)	0 (0 to 100)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Ciclesonide 40 µg Intent-to-Treat (ITT) v Placebo ITT
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [7]
Method	Wilcoxon (Mann-Whitney)

Notes:

[7] - One-sided p-value for superiority, significance level 2.5%.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Ciclesonide 80 µg ITT v Placebo ITT

Number of subjects included in analysis	455
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006 [8]
Method	Wilcoxon (Mann-Whitney)

Notes:

[8] - One-sided p-value for superiority, significance level 2.5%.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Ciclesonide 160 µg ITT v Placebo ITT
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [9]
Method	Wilcoxon (Mann-Whitney)

Notes:

[9] - One-sided p-value for superiority, significance level 2.5%.

Secondary: Change from Baseline in Lung Function Variable Forced Expiratory Volume in One Second (FEV1)

End point title	Change from Baseline in Lung Function Variable Forced Expiratory Volume in One Second (FEV1)

End point description:

Spirometry was performed according to local standards. FEV1 is the maximal amount of air forcefully exhaled from the lungs in one second. Higher change numbers indicate better lung function.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	270	281	270	124
Units: liters				
least squares mean (standard error)	0.123 (± 0.015)	0.122 (± 0.015)	0.139 (± 0.015)	0.039 (± 0.022)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Lung Function Variable PEF by Spirometry

End point title	Change from Baseline in Lung Function Variable PEF by Spirometry

End point description:

Spirometry was performed according to local standards. PEF is the maximum speed of expiration.

Analysis was ANCOVA with factors value at Baseline, treatment, age, sex, center pool, ICS pretreatment, spacer use and asthma severity. Higher change numbers indicate better lung function.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	270[10]	281[11]	272[12]	124[13]
Units: liters/minute				
least squares mean (standard error)	20.68 (± 2.61)	21.71 (± 2.51)	22.25 (± 2.61)	15.13 (± 3.69)

Notes:

[10] - Last observation carried forward (LOCF)

[11] - LOCF

[12] - LOCF

[13] - LOCF

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Morning PEF from Diary

End point title	Change from Baseline in Morning PEF from Diary

End point description:

PEF is the maximum speed of expiration. A portable electronic PEF meter was used for the home PEF readings. The patients recorded PEF daily, in the morning immediately after getting up. Readings were done preferably at least 4 hours after use of rescue medication and before inhalation of the study medication. At each measurement, three readings were obtained in the standing position. All three values were recorded in the diary; the highest value was used for evaluation. The higher change from Baseline values are the best. Analysis of covariance (ANCOVA) model with the Baseline value and age as covariates was used for analysis.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1 thru 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304	312	311	146
Units: liters/minute				
least squares mean (standard error)				
Change at Week 1 (n=303,311,310,146)	11.61 (± 1.55)	9.2 (± 1.5)	11.54 (± 1.54)	4.54 (± 2.13)
Change at Week 2 (n=303,311,310,146)	9.82 (± 1.89)	11.95 (± 1.83)	12.26 (± 1.89)	4.2 (± 2.61)
Change at Week 3 (n=304,312,310,146)	11.36 (± 2.08)	11.11 (± 2.01)	13.15 (± 2.07)	6.74 (± 2.87)

Change at Week 4 (n=304,312,310,146)	13.63 (± 2.18)	13.27 (± 2.12)	15.6 (± 2.18)	6.31 (± 3.02)
Change at Week 5	14.86 (± 2.23)	13.33 (± 2.16)	15.39 (± 2.22)	9.67 (± 3.08)
Change at Week 6	13.91 (± 2)	13.26 (± 2.23)	14.71 (± 2.29)	7.64 (± 3.18)
Change at Week 7	14.57 (± 2.37)	15.05 (± 2.3)	14.14 (± 2.36)	6.21 (± 3.28)
Change at Week 8	14.57 (± 2.39)	15.92 (± 2.31)	13.63 (± 2.38)	7.05 (± 3.3)
Change at Week 9	15.26 (± 2.44)	16.02 (± 2.36)	13.23 (± 2.43)	7.88 (± 3.37)
Change at Week 10	16.35 (± 2.48)	16.79 (± 2.4)	14.59 (± 2.47)	7.66 (± 3.43)
Change at Week 11	16.12 (± 2.6)	15.97 (± 2.52)	16.24 (± 2.59)	6.8 (± 3.6)
Change at Week 12	15.93 (± 2.72)	15.43 (± 2.64)	17.59 (± 2.71)	6.41 (± 3.76)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Evening PEF from Diary

End point title	Change from Baseline in Evening PEF from Diary

End point description:

PEF is the maximum speed of expiration. A portable electronic PEF meter was used for the home PEF readings. The patients recorded PEF daily, in the morning immediately after getting up. Readings were done preferably at least 4 hours after use of rescue medication and before inhalation of the study medication. At each measurement, three readings were obtained in the standing position. All three values were recorded in the diary; the highest value was used for evaluation. The higher change from Baseline values are the best. Analysis of covariance (ANCOVA) model with the Baseline value and age as covariates was used for analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304[14]	312[15]	310[16]	146[17]
Units: liters/minute				
least squares mean (standard error)	10.16 (± 2.54)	9.37 (± 2.46)	12.71 (± 2.53)	4.02 (± 3.52)

Notes:

[14] - LOCF

[15] - LOCF

[16] - LOCF

[17] - LOCF

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Diurnal PEF Fluctuations

End point title	Change from Baseline in Diurnal PEF Fluctuations

End point description:

PEF is the maximum speed of expiration. A portable electronic PEF meter was used for the home PEF readings. The patients recorded PEF daily, in the morning immediately after getting up. Readings were done preferably at least 4 hours after use of rescue medication and before inhalation of the study medication. At each measurement, three readings were obtained in the standing position. All three values were recorded in the diary; the highest value was used for evaluation. A negative change from Baseline indicates improvement. Analysis of covariance (ANCOVA) model with the Baseline value and age as covariates was used for analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	303	312	310	146
Units: percent change				
arithmetic mean (standard deviation)	-0.841 (± 9.942)	-1.209 (± 10.686)	-1.192 (± 11.29)	0.214 (± 9.453)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Asthma Symptom Total Score

End point title	Change in Asthma Symptom Total Score

End point description:

Measurements of both nighttime and daytime asthma symptoms were assessed on a daily basis by the patient in the electronic diary, according to the following scales: Nighttime Asthma Score using a 5 point scale: 0=no asthma symptoms, slept through the night to 4=bad night, awake most of the night because of asthma. Daytime Asthma Score using a 5 point scale: 0=very well, no asthma symptoms to 4=asthma very bad, unable to carry out daily activities as usual. Total possible overall daily score range from 0 (best) to 4 (worst). A negative change from Baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304[18]	312[19]	311[20]	146[21]
Units: score on a scale				
arithmetic mean (standard deviation)				
Asthma Total Symptom Score (n=304,312,310,146)	-0.916 (± 1.265)	-0.983 (± 1.209)	-0.879 (± 1.27)	-0.572 (± 1.483)
Asthma Daytime Symptom Score (n=304,312,310,146)	-0.529 (± 0.682)	-0.553 (± 0.721)	-0.517 (± 0.662)	-0.354 (± 0.801)

Asthma Nighttime Symptom Score	-0.392 (± 0.775)	-0.435 (± 0.672)	-0.35 (± 0.791)	-0.233 (± 0.858)

Notes:

[18] - LOCF

[19] - LOCF

[20] - LOCF

[21] - LOCF

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Use of Rescue Medications

End point title	Change in Use of Rescue Medications

End point description:

The daily use of rescue medication (salbutamol) was recorded in the electronic diary in the morning and the evening. A negative change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	304[22]	312[23]	311[24]	146[25]
Units: puffs/day				
arithmetic mean (standard deviation)	-0.872 (± 1.634)	-0.999 (± 1.532)	-0.886 (± 1.771)	-0.527 (± 1.931)

Notes:

[22] - LOCF

[23] - LOCF

[24] - LOCF

[25] - LOCF

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Days with Asthma Control Based on Symptoms, Use of Rescue Medication and Morning PEF

End point title	Percentage of Days with Asthma Control Based on Symptoms, Use of Rescue Medication and Morning PEF

End point description:

Control of asthma was evaluated on a daily basis (24 hours) using the following variables: asthma symptoms, use of rescue medication, and morning (am) PEF . The median percentage of days with asthma control is presented.

End point type	Secondary

End point timeframe:

28 days prior to last visit (Up to 12 Weeks)

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	302	311	309	144
Units: percentage of days				
median (full range (min-max))	8.33 (0 to 100)	13.64 (0 to 100)	13.04 (0 to 100)	0 (0 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pediatric Asthma Quality of Life Questionnaire Standard [PAQLQ(S)] Overall Score

End point title	Change from Baseline in Pediatric Asthma Quality of Life Questionnaire Standard [PAQLQ(S)] Overall Score

End point description:

PAQLQS is a disease specific instrument to assess the impact of asthma on the patient's quality of life. The PAQLQS consists of 23 items in 3 domains evaluating activity limitations, symptoms and emotional function. Patients answered each question using a 7-point scale from 1= maximum impairment to 7=no impairment) about their experience during the previous week. Total possible score ranging from 23 (worst) to 161(best). Higher change from Baseline scores are the best. Analysis of covariance (ANCOVA) model with the baseline value and age as covariates was used for analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	167	179	171	76
Units: score on a scale				
least squares mean (standard error)	0.78 (± 0.07)	0.71 (± 0.007)	0.72 (± 0.07)	0.43 (± 0.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pediatric asthma Caregiver's Quality of Life Questionnaire (PACQLQ) Overall

End point title	Change from Baseline in Pediatric asthma Caregiver's Quality of Life Questionnaire (PACQLQ) Overall

End point description:

PACQLQ assesses the impact of the child’s asthma on the quality of life of the caregiver. The PACQLQ consists of 13 items in 2 domains evaluating activity limitations and emotional function. Caregivers answered each question using a 7-point scale from 1= maximum impairment to 7=no impairment about their experience during the previous week. Total possible score ranging from 13 (worst) to 91(best). Higher change from Baseline scores are the best. Analysis of covariance (ANCOVA) model with the baseline value and age as covariates was used for analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Ciclesonide 40 µg Intent-to-Treat (ITT)	Ciclesonide 80 µg ITT	Ciclesonide 160 µg ITT	Placebo ITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	169	177	172	74
Units: score on a scale				
least squares mean (standard error)	0.82 (± 0.08)	0.88 (± 0.08)	0.84 (± 0.08)	0.71 (± 0.12)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug to 30 days after last dose of study drug (Up to 20 Weeks)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Ciclesonide 40 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a metered-dose inhaler (MDI), once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 80 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 40 µg, inhaled via a MDI, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Ciclesonide 160 µg

Reporting group description:

Placebo-matching ciclesonide, inhaled via a MDI, once daily, in the evening for 2 to 4 weeks in the Baseline period followed by ciclesonide 160 µg, inhaled via a MDI, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Reporting group title	Placebo

Reporting group description:

Placebo-matching Ciclesonide ,inhaled via a MDI, once daily in the evening for 2 to 4 week in the Baseline period followed by placebo-matching ciclesonide, inhaled via a MDI, once daily in the evening for 12 weeks. Salbutamol 100 µg/puff was available to be used as rescue medication if needed.

Serious adverse events	Ciclesonide 40 µg	Ciclesonide 80 µg	Ciclesonide 160 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 305 (1.31%)	5 / 312 (1.60%)	2 / 310 (0.65%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Open wound			
subjects affected / exposed	0 / 305 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 312 (0.00%)	0 / 310 (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
Nervous system disorders			
Tremor			
subjects affected / exposed	0 / 305 (0.00%)	0 / 312 (0.00%)	0 / 310 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 305 (0.33%)	2 / 312 (0.64%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 312 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 305 (0.00%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 305 (0.33%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 305 (0.33%)	1 / 312 (0.32%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis streptococcal			
subjects affected / exposed	1 / 305 (0.33%)	0 / 312 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 146 (0.68%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Open wound			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tremor			
subjects affected / exposed	1 / 146 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis streptococcal			
subjects affected / exposed	0 / 146 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ciclesonide 40 µg	Ciclesonide 80 µg	Ciclesonide 160 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 305 (16.07%)	45 / 312 (14.42%)	45 / 310 (14.52%)
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	19 / 305 (6.23%)	10 / 312 (3.21%)	13 / 310 (4.19%)
occurrences (all)	22	10	15
Pharyngitis			
subjects affected / exposed	14 / 305 (4.59%)	18 / 312 (5.77%)	16 / 310 (5.16%)
occurrences (all)	14	19	19
Upper respiratory tract infection			
subjects affected / exposed	18 / 305 (5.90%)	20 / 312 (6.41%)	16 / 310 (5.16%)
occurrences (all)	21	21	16

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 146 (9.59%)		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 146 (2.05%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	7 / 146 (4.79%)		
occurrences (all)	8		
Upper respiratory tract infection			
subjects affected / exposed	5 / 146 (3.42%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2006	• Mean PEF criterion regarding the minimum number of days with morning measurements defined. • Clarification of LOE criteria • Added calculation of PEF reversibility.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported