Clinical trial results:
Effect of Low Dose Continuous Treatment with Ciclesonide over One Year on the Time to First Exacerbation in Children with Mild Asthma Versus Intermittent Treatment for Exacerbations

Summary

EudraCT number	2007-003736-34
Trial protocol	HU
Global end of trial date	25 June 2009

Results information

Result version number	v1 (current)
This version publication date	28 May 2017
First version publication date	28 May 2017

Trial information

Trial identification

Sponsor protocol code	BY9010/CA-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00163293
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	AstraZeneca Clinical Study Information Center, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	AstraZeneca Clinical Study Information Center, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	25 June 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2009
Global end of trial reached?	Yes
Global end of trial date	25 June 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to compare the efficacy of ciclesonide with respect to reduction of the number of asthma exacerbations in children with mild persistent asthma. Treatment medication will be administered as follows: ciclesonide will be inhaled once daily, using one of the two dose levels versus placebo together with other corticosteroids used as intermittent treatment. The study duration consists of a baseline period (3 to 4 weeks) and a treatment period (12 months). The study will provide further data on safety and tolerability of ciclesonide.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 January 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 142
Country: Number of subjects enrolled	Hungary: 39
Country: Number of subjects enrolled	South Africa: 59
Worldwide total number of subjects	240
EEA total number of subjects	39

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)	240
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 30 investigative sites in Canada, Hungary and South Africa from 24 January 2005 to 25 June 2009.

Pre-assignment

Screening details:

Children who experienced symptoms consistent with mild asthma for at least 12 months were enrolled in 1 of 3 treatment groups: once a day placebo, 100 µg or 200 µg ciclesonide.

Pre-assignment period milestones

Number of subjects started	240
Number of subjects completed	239

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not receive study drug.: 1

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, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Ciclesonide 100 µg

Arm description:

Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

Arm type	Experimental
Investigational medicinal product name	Ciclesonide 100 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

50 µg two puffs once daily, in the evening via a metered-dose inhaler (50 µg ex-valve corresponds to 40 µg ex-actuator)

Arm title	Ciclesonide 200 µg

Arm description:

Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

Arm type	Experimental
Investigational medicinal product name	Ciclesonide 200 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

100 µg two puffs once daily, in the evening via a metered-dose inhaler (100 µg ex-valve corresponds to 80 µg ex-actuator)

Arm title	Placebo

Arm description:

Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

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

Dosage and administration details:

two puffs once daily, in the evening, via a metered-dose inhaler

Number of subjects in period 1[1]	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo
Started	79	76	84
Completed	66	69	66
Not completed	13	7	18
Reasons Not Specified	13	7	18

Notes:

[1] - 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: 240 patients were randomized but only 239 were treated.

Baseline characteristics

Reporting groups	
Reporting group title	Ciclesonide 100 µg
Reporting group description:	
Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	
Reporting group title	Ciclesonide 200 µg
Reporting group description:	
Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	
Reporting group title	Placebo
Reporting group description:	
Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	

Reporting group values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo
Number of subjects	79	76	84
Age categorical Units: Subjects			
Children (2-11 years)	79	76	84
Age Continuous Units: years			
arithmetic mean	7.9	7.7	8.1
standard deviation	± 2.06	± 1.84	± 2.19
Gender, Male/Female Units: participants			
Female	33	31	34
Male	46	45	50
Race/Ethnicity, Customized Units: Subjects			
Asian	6	6	6
Black	4	2	5
Caucasian	55	53	59
Other	14	15	14
Smoking Classification Units: Subjects			
Non-Smokers	79	76	84
Study Specific Characteristic | Weight			
Weight data was only available for n=77, 76, 84 participants, respectively.			
Units: kg			
arithmetic mean	29.9	30.01	33.13
standard deviation	± 9.701	± 9.247	± 11.64
Study Specific Characteristic | Body Mass Index (BMI)			
BMI data was only available for n=77, 76, 84 participants, respectively.			
Units: kg/m^2			
arithmetic mean	17.3	17.69	18.68
standard deviation	± 3.107	± 2.977	± 4.069

Reporting group values	Total		

Number of subjects	239		
Age categorical Units: Subjects			
Children (2-11 years)	239		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender, Male/Female Units: participants			
Female	98		
Male	141		
Race/Ethnicity, Customized Units: Subjects			
Asian	18		
Black	11		
Caucasian	167		
Other	43		
Smoking Classification Units: Subjects			
Non-Smokers	239		
Study Specific Characteristic | Weight			
Weight data was only available for n=77, 76, 84 participants, respectively.			
Units: kg arithmetic mean standard deviation	 -		
Study Specific Characteristic | Body Mass Index (BMI)			
BMI data was only available for n=77, 76, 84 participants, respectively.			
Units: kg/m^2 arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Ciclesonide 100 µg
Reporting group description:	
Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	
Reporting group title	Ciclesonide 200 µg
Reporting group description:	
Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	
Reporting group title	Placebo
Reporting group description:	
Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.	

Primary: Time to First Asthma Exacerbation

End point title	Time to First Asthma Exacerbation
End point description:	
Time to first asthma exacerbation is defined as the time in days until the first asthma exacerbation, or to the end of treatment visit. In the absence of an exacerbation, an early treatment discontinuation is treated as a censored observation on the day following the last use of study drug. Intention to Treat (ITT) analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.	
End point type	Primary
End point timeframe:	
Up to 12 months	

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: days				
arithmetic mean (standard error)	225.1 (± 14.73)	249.5 (± 14.79)	227.2 (± 15.2)	

Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Ciclesonide 100 µg v Placebo
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6625
Method	Logrank

Statistical analysis title	Analysis 2
Comparison groups	Ciclesonide 200 µg v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7303
Method	Logrank

Primary: Exacerbations (Post-hoc Analysis of Annual Rates)

End point title	Exacerbations (Post-hoc Analysis of Annual Rates)

End point description:

A model-based analysis of asthma exacerbation was performed to adjust to important covariables. The distribution of the data suggested a Poisson regression modeling (zero inflated) strategy. After a variable selection process considering also variable-by-treatment interactions, the variables centre, age [years] and race were identified to be important beside treatment. The parameters centre and age [years] were allocated to zero-model part and the variables treatment and race to the Poisson model part. The estimates of the per-treatment rates are based on a negative-binomial distribution. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

End point type	Primary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: number of events per year				
least squares mean (standard error)	0.9343 (± 0.2909)	0.8794 (± 0.2747)	1.2621 (± 0.2768)	

Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Ciclesonide 100 µg v Placebo
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1291 [1]
Method	Wald Chi-square

Notes:

[1] - zero inflated Poisson model: adjustment for centre and age [yrs] (zero model), treatment and race (Poisson model)

Statistical analysis title	Analysis 2
Comparison groups	Ciclesonide 200 µg v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0145 [2]
Method	Wald Chi-square

Notes:

[2] - zero inflated Poisson model: adjustment for centre and age [yrs] (zero model), treatment and race (Poisson model)

Secondary: Growth Velocity as Assessed by Stadiometric Height Measurement

End point title	Growth Velocity as Assessed by Stadiometric Height Measurement

End point description:

Standing height measured in millimeters (mm) with a wall-mounted stadiometer. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: mm/year				
arithmetic mean (standard deviation)	55.32 (± 25.81)	64.6 (± 27.31)	54.91 (± 21.78)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Rate of Asthma Exacerbations per Year

End point title	Mean Rate of Asthma Exacerbations per Year

End point description:

Rate of asthma exacerbations per year is equal to total number of asthma exacerbations during treatment/time on treatment (year). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: number of exacerbations per year				
arithmetic mean (standard deviation)	0.88 (± 1.366)	0.85 (± 1.31)	3.28 (± 19.874)	

Statistical analyses

Statistical analysis title	Analysis 2
Comparison groups	Ciclesonide 200 µg v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6844
Method	Kruskal-wallis

Statistical analysis title	Analysis 1
Comparison groups	Ciclesonide 100 µg v Placebo
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4754
Method	Kruskal-wallis

Secondary: Duration of Exacerbations

End point title	Duration of Exacerbations

End point description:

Duration of exacerbation was defined as the time in days when the criteria for an exacerbation were met to the time when peak flow measurements returned to baseline. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: days				
arithmetic mean (standard deviation)	9.17 (± 6.198)	9.31 (± 7.65)	7.92 (± 4.061)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Exacerbations per Participant

End point title	Number of Exacerbations per Participant

End point description:

The mean number of asthma exacerbations per participant is reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: exacerbations				
arithmetic mean (standard deviation)	0.72 (± 1.025)	0.78 (± 1.028)	0.95 (± 1.316)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Dropped-out due to Asthma Exacerbation

End point title	Percentage of Participants who Dropped-out due to Asthma Exacerbation

End point description:

ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percentage of participants				
number (not applicable)	1.3	1.3	4.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Absolute Value)

End point title	Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Absolute Value)

End point description:

FEV1 is the maximal amount of air forcefully exhaled from the lungs in one second. Spirometry was used for assessment of FEV1. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: liters				
arithmetic mean (standard deviation)				
Change at Month 1 (n=78, 76, 81)	0.019 (± 0.1715)	0.018 (± 0.1639)	0.012 (± 0.1627)	
Change at Month 2 (n=76, 73, 77)	0.024 (± 0.1416)	0.06 (± 0.1582)	0.005 (± 0.1416)	
Change at Month 4 (n=68, 72, 75)	0.065 (± 0.1483)	0.083 (± 0.1486)	0.076 (± 0.1725)	
Change at Month 6 (n=67, 72, 72)	0.091 (± 0.1714)	0.125 (± 0.1975)	0.078 (± 0.1855)	
Change at Month 8 (n=66, 71, 68)	0.075 (± 0.2144)	0.126 (± 0.2089)	0.12 (± 0.1855)	
Change at Month 10 (n=66, 69, 67)	0.143 (± 0.1458)	0.168 (± 0.191)	0.146 (± 0.1609)	
Change at Month 12 (n=65, 69, 65)	0.161 (± 0.2022)	0.185 (± 0.2024)	0.178 (± 0.1593)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Percent Predicted)

End point title	Change From Baseline in Forced Expiratory Volume in one Second (FEV1) (Percent Predicted)

End point description:

FEV1 is the maximal amount of air forcefully exhaled from the lungs in one second. Spirometry was used for assessment of FEV1. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percent predicted FEV1				
arithmetic mean (standard deviation)				
Change at Month 1 (n=78, 76, 81)	1 (± 10.96)	0.6 (± 9.67)	1 (± 9.06)	
Change at Month 2 (n=76, 73, 77)	1.4 (± 8.5)	3.4 (± 9.6)	0.3 (± 8.05)	
Change at Month 4 (n=68, 72, 75)	4 (± 8.69)	4.6 (± 9.31)	5.1 (± 9.83)	
Change at Month 6 (n=67, 72, 72)	5.5 (± 10)	7.2 (± 11.35)	4.9 (± 10.93)	
Change at Month 8 (n=66, 71, 68)	4.4 (± 12.44)	6.5 (± 12.25)	7.1 (± 10.24)	
Change at Month 10 (n=66, 69, 67)	8.6 (± 9.41)	9.1 (± 10.48)	8.7 (± 9.22)	
Change at Month 12 (n=65, 69, 65)	9.5 (± 10.96)	10.1 (± 11.29)	10.4 (± 9.89)	

Statistical analyses

No statistical analyses for this end point

Secondary: Morning and Evening Peak Expiratory Flow (PEF) Measurements by Diary Entries

End point title	Morning and Evening Peak Expiratory Flow (PEF) Measurements by Diary Entries

End point description:

PEF is the maximum speed of expiration. Spirometry was used for assessment of PEF. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: liters/second				
arithmetic mean (standard deviation)				
Month 1, Evening PEF (n=78, 76, 80)	235.72 (± 63.882)	238.16 (± 52.565)	241.89 (± 70.619)	
Month 1, Morning PEF (n=78, 76, 81)	232.09 (± 64.933)	234.41 (± 52.908)	233.81 (± 66.039)	
Month 2, Evening PEF (n=76, 71, 77)	241.07 (± 58.604)	241.16 (± 50.422)	244.67 (± 67.846)	
Month 2, Morning PEF (n=76, 72, 77)	236.92 (± 61.243)	236.42 (± 52.323)	239.07 (± 70.132)	
Month 4, Evening PEF (n=68, 72, 75)	249.75 (± 58.528)	243.52 (± 49.076)	245.91 (± 65.802)	
Month 4, Morning PEF (n=68, 71, 76)	242.93 (± 56.658)	241.91 (± 48.498)	240.16 (± 65.211)	
Month 6, Evening PEF (n=67, 72, 73)	251.88 (± 60.255)	249.36 (± 59.294)	246.44 (± 63.946)	
Month 6, Morning PEF (n=67, 72, 73)	246.44 (± 59.781)	246.75 (± 60.02)	238.81 (± 63.419)	
Month 8, Evening PEF (n=66, 70, 69)	253.49 (± 59.666)	250.92 (± 51.376)	245.72 (± 61.399)	
Month 8, Morning PEF (n=66, 71, 69)	247.24 (± 59.806)	246.97 (± 51.592)	239.73 (± 61.733)	
Month 10, Evening PEF (n=65, 70, 68)	254.21 (± 56.815)	256.44 (± 56.469)	251.69 (± 60.704)	
Month 10, Morning PEF (n=66, 70, 68)	247.94 (± 60.418)	254.04 (± 56.719)	246.23 (± 62.805)	
Month 12, Evening PEF (n=68, 71, 70)	255.97 (± 57.291)	263.87 (± 58.469)	261.88 (± 61.383)	
Month 12, Morning PEF (n=75, 73, 78)	245.84 (± 59.834)	258.62 (± 57.009)	250.55 (± 63.204)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PEF by Diary Entries

End point title	Change From Baseline in PEF by Diary Entries

End point description:

PEF is the maximum speed of expiration. Spirometry was used for assessment of PEF. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: liters/second				
arithmetic mean (standard deviation)				
Change at Month 1, Evening PEF (n=78, 76, 80)	8.46 (± 17.952)	8.54 (± 19.474)	6.06 (± 39.183)	
Change at Month 1, Morning PEF (n=78, 76, 81)	11.69 (± 21.268)	10.82 (± 20.372)	7.54 (± 25.697)	
Change at Month 2, Evening PEF (n=76, 71, 77)	13.66 (± 28.491)	13.04 (± 20.89)	10.83 (± 40.563)	
Change at Month 2, Morning PEF (n=76, 72, 77)	17.12 (± 32.068)	14.3 (± 22.649)	14.29 (± 37.228)	
Change at Month 4, Evening PEF (n=68, 72, 75)	20.41 (± 22.058)	16.01 (± 21.547)	13.62 (± 37.99)	
Change at Month 4, Morning PEF (n=68, 71, 76)	21.33 (± 26.603)	18.24 (± 22.808)	16.28 (± 34.841)	
Change at Month 6, Evening PEF (n=67, 72, 73)	22.44 (± 28.236)	21.86 (± 38.28)	13.14 (± 33.321)	
Change at Month 6, Morning PEF (n=67, 72, 73)	24.82 (± 30.613)	24.68 (± 40.981)	14.44 (± 29.95)	
Change at Month 8, Evening PEF (n=66, 70, 69)	25.47 (± 27.43)	21.38 (± 28.648)	13.3 (± 37.061)	
Change at Month 8, Morning PEF (n=66, 71, 69)	27.16 (± 32.53)	23.76 (± 29.089)	16.03 (± 34.017)	
Change at Month 10, Evening PEF (n=65, 70, 68)	25.68 (± 30.945)	26.78 (± 34.255)	18.04 (± 38.209)	
Change at Month 10, Morning PEF (n=66, 70, 68)	27.86 (± 38.406)	29.84 (± 36.39)	21.25 (± 34.94)	
Change at Month 12, Evening PEF (n=68, 71, 70)	28.24 (± 28.811)	33.35 (± 38.772)	25.38 (± 43.284)	
Change at Month 12, Morning PEF (n=75, 73, 78)	26.84 (± 32.932)	34.31 (± 41.166)	24.37 (± 39.312)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Diurnal PEF Fluctuation

End point title	Change From Baseline in Diurnal PEF Fluctuation

End point description:

Diurnal PEF Fluctuation is equal to [(Higher PEF – Lower PEF)/0.5*(Higher PEF + Lower PEF)] * 100%. A positive change from Baseline indicates improvement. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percent fluctuation				
arithmetic mean (standard deviation)				
Change at Month 1 (n=78, 76, 80)	-0.59 (± 3.97)	0.06 (± 3.772)	0 (± 3.867)	
Change at Month 2 (n=76, 71, 77)	-0.13 (± 5.009)	-0.16 (± 4.131)	0.15 (± 5.084)	
Change at Month 4 (n=68, 71, 75)	-0.65 (± 5.251)	-1.01 (± 3.784)	-0.55 (± 4.421)	
Change at Month 6 (n=67, 72, 73)	-1.01 (± 4.351)	-0.22 (± 5.86)	-0.47 (± 4.28)	
Change at Month 8 (n=66, 70, 69)	-1.12 (± 4.83)	-1.21 (± 3.757)	-1.11 (± 4.048)	
Change at Month 10 (n=64, 70, 68)	-1.46 (± 5.221)	-0.7 (± 4.319)	-1.14 (± 4.059)	
Change at Month 12 (n=68, 70, 70)	-1.81 (± 4.913)	-0.62 (± 4.44)	-1.26 (± 4.187)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Asthma Symptom Score by Diary Entries

End point title	Total Asthma Symptom Score by Diary Entries

End point description:

Total Asthma Score=daytime asthma score + night-time asthma score, where higher score indicates worsening of disease. Night-time asthma score is assessed on a 5 point scale where 0=No symptoms, slept through the night, 1=Slept well but some complaints in the morning, 2=Woke up once because of asthma (including early wakening), 3=Woke up several times because of asthma (including early wakening) and 4=Bad night, awake most of the night because of asthma. Day-time asthma score is assessed on a 5 point scale where 0=Very well, no symptoms, 1=one episode of wheezing, cough or breathlessness, 2=More than 1 episode of wheezing, cough or breathlessness without interfering with normal activities, 3=Wheezing, cough or shortness of breath most of the day which interfered to some extent with normal activities and 4=Asthma very bad. Unable to carry out daily activities as usual. ITT analysis. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: score on a scale				
arithmetic mean (standard deviation)				
Month 1 (n=77, 75, 79)	0.37 (± 0.489)	0.22 (± 0.329)	0.32 (± 0.535)	

Month 2 (n=76, 70, 77)	0.26 (± 0.424)	0.14 (± 0.246)	0.28 (± 0.484)	
Month 4 (n=68, 72, 75)	0.18 (± 0.342)	0.12 (± 0.178)	0.24 (± 0.359)	
Month 6 (n=67, 72, 73)	0.16 (± 0.289)	0.17 (± 0.294)	0.18 (± 0.289)	
Month 8 (n=66, 69, 69)	0.17 (± 0.283)	0.13 (± 0.243)	0.23 (± 0.414)	
Month 10 (n=64, 70, 68)	0.12 (± 0.253)	0.11 (± 0.227)	0.24 (± 0.49)	
Month 12 (n=68, 69, 70)	0.11 (± 0.24)	0.08 (± 0.129)	0.15 (± 0.338)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Nights with Nocturnal Awakenings due to Asthma Symptoms

End point title	Percentage of Nights with Nocturnal Awakenings due to Asthma Symptoms

End point description:

Nocturnal awakenings due to asthma symptoms were recorded in the participant's diary. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percentage of nights				
arithmetic mean (standard deviation)				
Month 1 (n=78, 75, 80)	2.4 (± 6.159)	1.64 (± 4.256)	1.85 (± 4.223)	
Month 2 (n=76, 73, 77)	1.96 (± 5.877)	0.62 (± 2.364)	1.73 (± 4.662)	
Month 4 (n=68, 72, 75)	1.33 (± 4.017)	0.86 (± 2.139)	1.54 (± 4.106)	
Month 6 (n=67, 72, 73)	0.87 (± 2.527)	1.51 (± 3.288)	1.26 (± 3.235)	
Month 8 (n=66, 70, 69)	1.62 (± 4.129)	1.05 (± 2.823)	1.82 (± 5.024)	
Month 10 (n=66, 70, 68)	1.93 (± 7.106)	0.59 (± 2.22)	1.88 (± 5.468)	
Month 12 (n=74, 73, 78)	0.41 (± 1.554)	1.84 (± 11.769)	0.53 (± 1.853)	

Statistical analyses

No statistical analyses for this end point

Secondary: Rescue Medication Use per Day

End point title	Rescue Medication Use per Day

End point description:

Salbutamol (100 µg/puff) was used as rescue medication according to the individual needs of the participant. Each use was documented in the participant's diary. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: puffs/day				
arithmetic mean (standard deviation)				
Month 1 (n=57, 51, 54)	1 (± 1.345)	0.83 (± 1.148)	0.87 (± 0.91)	
Month 2 (n=53, 40, 46)	0.99 (± 1.296)	0.53 (± 0.728)	0.97 (± 1.298)	
Month 4 (n=48, 47, 51)	0.88 (± 1.3)	1.18 (± 1.595)	1.27 (± 1.984)	
Month 6 (n=45, 43, 44)	0.79 (± 1.084)	1.07 (± 1.329)	0.92 (± 1.583)	
Month 8 (n=38, 42, 45)	1.01 (± 1.53)	1.13 (± 1.95)	0.97 (± 1.219)	
Month 10 (n=38, 41, 39)	0.93 (± 1.423)	0.95 (± 1.243)	0.83 (± 1.113)	
Month 12 (n=36, 40, 40)	0.71 (± 0.897)	1.01 (± 1.36)	0.75 (± 1.152)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Rescue Medication Free Days

End point title	Percentage of Rescue Medication Free Days

End point description:

Days without use of rescue medication documented in the participant's diary were reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percentage of days				
arithmetic mean (standard deviation)				

Month 1 (n=55, 53, 54)	47.94 (± 44.405)	47.34 (± 44.984)	44.37 (± 45.367)	
Month 2 (n=52, 41, 48)	48.78 (± 46.442)	54.46 (± 46.668)	45.31 (± 47.761)	
Month 4 (n=49, 48, 52)	49.91 (± 48.274)	46.51 (± 45.209)	45.91 (± 46.328)	
Month 6 (n=47, 44, 45)	49.63 (± 48.084)	48.14 (± 45.321)	49.42 (± 47.515)	
Month 8 (n=39, 42, 44)	47.93 (± 45.17)	50.5 (± 46.1)	45.22 (± 45.002)	
Month 10 (n=40, 40, 37)	46.22 (± 47.901)	49.78 (± 48.521)	52.7 (± 46.015)	
Month 12 (n=35, 41, 40)	53.58 (± 47.785)	53.63 (± 48.358)	58.03 (± 46.264)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Asthma Symptom Free Days

End point title	Percentage of Asthma Symptom Free Days

End point description:

Days without Asthma Symptom documented in the participant's diary were reported. ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 1, 2, 4, 6, 8, 10 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: percentage of days				
arithmetic mean (standard deviation)				
Month 1 (n=62, 60, 60)	37.32 (± 40.983)	36.95 (± 42.207)	35 (± 43.032)	
Month 2 (n=61, 50, 56)	38.47 (± 44.743)	41.16 (± 44.738)	33.56 (± 44.161)	
Month 4 (n=54,55, 59)	42.57 (± 46.573)	38.83 (± 44.042)	35.78 (± 43.538)	
Month 6 (n=53, 50, 51)	41.75 (± 46.474)	39.87 (± 43.744)	40.09 (± 45.274)	
Month 8 (n=46, 46, 46)	38.86 (± 43.312)	43.9 (± 45.377)	40.03 (± 43.369)	
Month 10 (n=43, 47, 44)	41 (± 46.575)	41.65 (± 47.435)	39.83 (± 44.332)	
Month 12 (n=42, 44, 45)	43.2 (± 46.787)	42.03 (± 47.093)	44.61 (± 46.12)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessments as per Paediatric Asthma Quality of Life Questionnaire, Standardized (PAQLQ[S])

End point title	Quality of Life Assessments as per Paediatric Asthma Quality of Life Questionnaire, Standardized (PAQLQ[S])

End point description:

The PAQLQ(S) consists of 23 items divided into three domains: Activity limitations (items 1-3, 19, 22); Symptoms (items 4, 6, 8, 10, 12, 14, 16, 18, 20, 23) and Emotional function (items 5, 7, 9, 11, 13, 15, 17, 21). Participants were asked to answer each question using a seven-point scale (where "1" indicated maximum impairment and "7" indicated no impairment) and recall their experience during the previous week. Overall PAQLQ score is equal to the mean of all 23 items for a total possible score 1 (worst) to 7 (best). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 2, 6 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: score on a scale				
arithmetic mean (standard deviation)				
Month 2 (n=70, 73, 75)	6.21 (± 0.979)	6.27 (± 0.878)	6.08 (± 1.031)	
Month 6 (n=65, 72, 72)	6.33 (± 0.874)	6.26 (± 0.982)	6.3 (± 0.933)	
Month 12 (n=64, 69, 65)	6.42 (± 0.786)	6.34 (± 0.946)	6.36 (± 0.824)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessments as per Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)

End point title	Quality of Life Assessments as per Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)

End point description:

The PACQLQ consists of 13 items divided into two domains: Activity limitations (items 2, 4, 6, 8) and Emotional function (items 1, 3, 5, 7, 9, 10, 11, 12, 13). Caregivers answered each question using a seven-point scale (whereby "1" indicated maximum impairment and "7" indicated no impairment) and recalled their experiences during the previous week. Overall PACQLQ score is equal to the mean of all 13

items for a total possible score of 1 (worst) to 7 (best). ITT analysis set included all participants of the full analysis set who received at least one dose of study medication and had at least one post-baseline measurement of the primary efficacy outcome. "n" in the category is the number of participants with data available at the given time-point.

End point type	Secondary

End point timeframe:

Months 2, 6 and 12

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: score on a scale				
arithmetic mean (standard deviation)				
Month 2 (n=73, 73, 76)	5.87 (± 1.196)	6.16 (± 1.033)	6.08 (± 1.078)	
Month 6 (n=67, 72, 73)	6.15 (± 1.005)	6.16 (± 1.115)	6.31 (± 0.927)	
Month 12 (n=66, 69, 66)	6.32 (± 0.849)	6.25 (± 0.712)	6.31 (± 0.899)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Vital Signs Findings

End point title	Number of Participants with Clinically Significant Vital Signs Findings

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure and heart rate in beats per minute (bpm). The investigator determined if the result was clinically significant based on the following criteria: Systolic Blood Pressure >130 mmHg or <80 mmHg or a >20 mmHg difference from Baseline; Diastolic Blood Pressure > 85 mmHg; and Resting Heart Rate >140 bpm or <60 bpm or a >30 bpm difference from Baseline. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Physical Examination Findings

End point title	Number of Participants with Clinically Significant Physical Examination Findings

End point description:

A thorough physical examination was performed consisting of examinations of the following body systems: (1) eyes; (2) ears, nose, throat; (3) lungs/thorax; (4) heart/cardiovascular system; (5) abdomen; (6) skin and mucosae; (7) nervous system; (8) lymph nodes; (9) musculo-skeletal system; (10) physical examinations other than body systems described in (1) to (9). The investigator determined if any of the findings were clinically significant. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Laboratory Values

End point title	Number of Participants with Clinically Significant Laboratory Values

End point description:

Clinically significant laboratory values were hematology and chemistry tests determined by the investigator to be clinically significant based on the following criteria: Hemoglobin <9.5 g/dL; Erythrocytes <3.0 x 10^6/µL or >6.5 x 10^6/µL; White Blood Count <3000/mm^3 or >20000/mm^3; serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), gamma-glutamyl transpeptidase (GGT), Total Bilirubin and Glucose >2 times Upper limit of Normal Range (ULNR); Alkaline Phosphatase and Creatine Kinase >3 times ULNR; Creatinine >1.5 times ULN; Potassium >5.0 mmol/L or <3.0 mmol/L; and Sodium >150 mmol/L or 130 mmol/L. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events and Serious Adverse Events

End point title	Number of Participants with Adverse Events and Serious Adverse Events

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A SAE is any untoward medical occurrence that at any dose results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in congenital anomaly/birth defect or any other important medical condition considered serious based on medical and scientific judgement. Safety analysis set included all randomized participants who received at least 1 dose of trial medication.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Ciclesonide 100 µg	Ciclesonide 200 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	76	84	
Units: participants				
Adverse Events	61	64	63	
Serious Adverse Events	2	2	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 months

Adverse event reporting additional description:

At each visit investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by participant or observed by investigator was recorded, irrespective of relation to treatment. All adverse events and serious adverse events were coded according to MedDRA versions 8.0, 8.1, 9.0 and 9.1.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Ciclesonide 100 µg

Reporting group description:

Ciclesonide 100 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

Reporting group title	Placebo

Reporting group description:

Ciclesonide placebo-matching, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

Reporting group title	Ciclesonide 200 µg

Reporting group description:

Ciclesonide 200 µg, metered-dose inhaler, two puffs once daily, in the evening, for up to 12 months.

Serious adverse events	Ciclesonide 100 µg	Placebo	Ciclesonide 200 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 79 (2.53%)	2 / 84 (2.38%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Myringoplasty			
subjects affected / exposed	0 / 79 (0.00%)	0 / 84 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 79 (0.00%)	1 / 84 (1.19%)	0 / 76 (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
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 79 (0.00%)	1 / 84 (1.19%)	0 / 76 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 79 (1.27%)	0 / 84 (0.00%)	0 / 76 (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
Epistaxis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 84 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 79 (0.00%)	1 / 84 (1.19%)	0 / 76 (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
Laryngitis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 84 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 79 (1.27%)	0 / 84 (0.00%)	0 / 76 (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

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

Non-serious adverse events	Ciclesonide 100 µg	Placebo	Ciclesonide 200 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 79 (70.89%)	56 / 84 (66.67%)	55 / 76 (72.37%)
Nervous system disorders			

Headache	Additional description: non-serious		
subjects affected / exposed	4 / 79 (5.06%)	8 / 84 (9.52%)	7 / 76 (9.21%)
occurrences (all)	6	10	10
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 79 (7.59%)	4 / 84 (4.76%)	2 / 76 (2.63%)
occurrences (all)	6	5	2
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: non-serious		
subjects affected / exposed	35 / 79 (44.30%)	39 / 84 (46.43%)	38 / 76 (50.00%)
occurrences (all)	60	82	64
Cough			
subjects affected / exposed	6 / 79 (7.59%)	6 / 84 (7.14%)	4 / 76 (5.26%)
occurrences (all)	8	7	10
Rhinitis allergic			
subjects affected / exposed	7 / 79 (8.86%)	4 / 84 (4.76%)	4 / 76 (5.26%)
occurrences (all)	7	6	4
Infections and infestations			
Ear infection			
subjects affected / exposed	5 / 79 (6.33%)	2 / 84 (2.38%)	3 / 76 (3.95%)
occurrences (all)	5	2	4
Influenza			
subjects affected / exposed	3 / 79 (3.80%)	3 / 84 (3.57%)	6 / 76 (7.89%)
occurrences (all)	3	3	8
Lower respiratory tract infection			
subjects affected / exposed	1 / 79 (1.27%)	1 / 84 (1.19%)	4 / 76 (5.26%)
occurrences (all)	1	1	4
Nasopharyngitis			
subjects affected / exposed	13 / 79 (16.46%)	14 / 84 (16.67%)	9 / 76 (11.84%)
occurrences (all)	20	30	18
Pharyngitis			
subjects affected / exposed	5 / 79 (6.33%)	4 / 84 (4.76%)	4 / 76 (5.26%)
occurrences (all)	5	5	5
Rhinitis			
subjects affected / exposed	4 / 79 (5.06%)	3 / 84 (3.57%)	0 / 76 (0.00%)
occurrences (all)	4	5	0

Sinusitis			
subjects affected / exposed	1 / 79 (1.27%)	5 / 84 (5.95%)	1 / 76 (1.32%)
occurrences (all)	2	7	1
Upper respiratory tract infection			
subjects affected / exposed	18 / 79 (22.78%)	16 / 84 (19.05%)	19 / 76 (25.00%)
occurrences (all)	28	35	31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2004	Amendment 1: • Addition of history of cataracts and/or glaucoma as an exclusion criterion due to the potential class effect of ocular disturbances with the long-term use of inhaled corticosteroid (ICS).
01 November 2004	Amendment 2: • Removal of the hyper-responsiveness test (challenge test) as a pre-randomisation requirement for study inclusion, • Dose for fluticasone propionate (FP) to be consistent with the marketed dosing of Flovent® and the standard in treatment (two puffs of 125 µg FP per day). • Inclusion of a guideline on inhalation technique for study medication that accommodated the full potential age range of participants enrolled in the trial. • Amendment of the paradigm for treatment of exacerbations to add a guideline on how to treat a participant who is getting better within 24 hours with regard to usage of FP. • Amendment of the study time table.
08 August 2005	Amendment 3:• Administrative change in personnel and contact information. • Changes referring to the use of intranasal medications for the treatment of rhinitis. • Exclusion criterion concerning use of topical steroids was originally implemented to limit any confounding variable. However, according to the literature available currently, no impact on growth or HPA axis has been demonstrated in many studies of topical nasal steroids.
10 March 2006	Amendment 4: Administrative changes to study personnel and contact information; submission to authorities; study protocol, documentation and archiving of data, and an increase in the number of study sites, reflecting the expansion of the trial to additional sites in countries other than Canada (Brazil and South Africa).
22 June 2007	Amendment 5: Administrative changes in the local sponsor and contact information reflecting a change in country of origin for study sites (from Canada, Brazil and South Africa to Canada, Hungary and South Africa). Change in study timelines.
17 January 2008	Amendment 6: Administrative changes to study timelines and local sponsor name and contact information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported