Clinical trial results:
A multicentre, randomized, double-blind, double-dummy, active-controlled, parallel-group study to determine the efficacy and safety of nebulized fluticasone propionate 1mg twice daily compared with oral prednisone administered for 7 days to Chinese pediatric and adolescent subjects (aged 4 to 16 years) with an acute exacerbation of asthma

Summary

EudraCT number	2015-004870-14
Trial protocol	Outside EU/EEA
Global end of trial date	21 June 2013

Results information

Result version number	v1 (current)
This version publication date	25 September 2016
First version publication date	25 September 2016

Trial information

Trial identification

Sponsor protocol code	LOC114220

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Clinical Support Help Desk, GlaxoSmithKline Research & Development Ltd, +44 08007839733, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Clinical Support Help Desk, GlaxoSmithKline Research & Development Ltd, +44 08007839733, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 June 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy and safety of nebulized fluticasone propionated 1mg BID compared with oral prednisone administered for 7 days to Chinese pediatric and adolescent subjects (aged 4 to 16 years) with an acute exacerbatio of asthma.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2012
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	China: 266
Worldwide total number of subjects	266
EEA total number of subjects	0

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)	259
Adolescents (12-17 years)	7
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study consisted of two periods: treatment period (7 days) and follow-up period (14 days). The total participation time in the study from Visit 1 (day of presentation to the clinic or emergency department with an acute exacerbation of asthma) to Visit 4 (follow-up phone contact) was approximately 21 days.

Pre-assignment

Screening details:

A total of 261 participants (par.) who presented to the clinical or emergency department with an acute exacerbation of asthma were enrolled in the study. A total of 251 participants received at least a single dose of investigational products (IP).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fluticasone propionate

Arm description:

Participants received fluticasone propionate (FP) inhalation solution twice daily 2x0.5 milligrams (mg)/milliliters (mL) via a nebulizer in morning and evening for 7 days. Participants also received placebo tablets once daily in the morning for 7 days. Salbutamol was provided on a needed basis throughout the treatment period.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Propionate Nebules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

2x0.5 mg/2mL twice daily via nebulization in morning and evening for 7 days

Investigational medicinal product name	Dummy tablet placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo soluble tablets once daily in the morning for 7 days.

Arm title	Prednisone

Arm description:

Participants received oral prednisone (Pred) tablets once daily at 2 mg per kilogram (kg) per day, up to 40 mg per day for 4 days, then 1 mg per kg per day or half of the original dose, up to 20 mg per day for 3 days in the morning. Participants also received placebo nebules 2×2mL 0.9% saline twice daily (in morning and evening) for 7 days. Salbutamol was provided on an needed basis throughout the treatment period.

Arm type	Active comparator

Investigational medicinal product name	Prednisone Tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg per kg per day once daily, up to 40mg per day for 4 Days, then 1 mg per kg per day or half of the original dose, up to 20 mg per day for 3 days in morning.

Investigational medicinal product name	Dummy nebules placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

2×2mL 0.9% saline twice daily for 7 Days in morning and evening

Number of subjects in period 1[1]	Fluticasone propionate	Prednisone
Started	123	128
Completed	116	123
Not completed	7	5
Consent withdrawn by subject	6	3
Lack of efficacy	1	1
Protocol deviation	-	1

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: A total of 266 subjects were screened for this study. A total of 261 participants (par.) who presented to the clinical or emergency department with an acute exacerbation of asthma were enrolled in the study. A total of 251 participants received at least a single dose of investigational products (IP).

Baseline characteristics

Reporting groups	
Reporting group title	Fluticasone propionate
Reporting group description:	
Participants received fluticasone propionate (FP) inhalation solution twice daily 2x0.5 milligrams (mg)/milliliters (mL) via a nebulizer in morning and evening for 7 days. Participants also received placebo tablets once daily in the morning for 7 days. Salbutamol was provided on a needed basis throughout the treatment period.	
Reporting group title	Prednisone
Reporting group description:	
Participants received oral prednisone (Pred) tablets once daily at 2 mg per kilogram (kg) per day, up to 40 mg per day for 4 days, then 1 mg per kg per day or half of the original dose, up to 20 mg per day for 3 days in the morning. Participants also received placebo nebules 2×2mL 0.9% saline twice daily (in morning and evening) for 7 days. Salbutamol was provided on an needed basis throughout the treatment period.	

Reporting group values	Fluticasone propionate	Prednisone	Total
Number of subjects	123	128	251
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	6.6	6.5	
standard deviation	± 2.41	± 2.32	-
Gender categorical Units: Subjects			
Female	51	51	102
Male	72	77	149
Race, Customized Units: Subjects			
Asian - East Asian Heritage	123	128	251

End points

End points reporting groups

Reporting group title	Fluticasone propionate

Reporting group description:

Participants received fluticasone propionate (FP) inhalation solution twice daily 2x0.5 milligrams (mg)/milliliters (mL) via a nebulizer in morning and evening for 7 days. Participants also received placebo tablets once daily in the morning for 7 days. Salbutamol was provided on a needed basis throughout the treatment period.

Reporting group title	Prednisone

Reporting group description:

Participants received oral prednisone (Pred) tablets once daily at 2 mg per kilogram (kg) per day, up to 40 mg per day for 4 days, then 1 mg per kg per day or half of the original dose, up to 20 mg per day for 3 days in the morning. Participants also received placebo nebules 2×2mL 0.9% saline twice daily (in morning and evening) for 7 days. Salbutamol was provided on an needed basis throughout the treatment period.

Primary: Mean morning (AM) peak expiratory flow (PEF) on diary card over the treatment assessment period (ITT Population)

End point title	Mean morning (AM) peak expiratory flow (PEF) on diary card over the treatment assessment period (ITT Population)

End point description:

PEF is the maximum flow generated during a forceful exhalation, starting from full lung inflation. Par. (if needed with the help of parents or guardian) recorded on diary card the best of three PEF measurements, using a mini-Wright peak flow meter in the morning before taking any study medication. Only data that was drawn from Days 2 to 8 after randomization and on or before one day after the end date of study drug was used for analysis. The endpoint was considered missing if less than 2 days were recorded in the given treatment assessment period. Two par. from fluticasone propionate group and 4 par. from prednisone group had the missing endpoint. Analysis was performed using an analysis of covariance (ANCOVA) model with effects due to gender, age, center and treatment group. Intent-to-Treat (ITT) Population: all par. randomized to treatment and who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Days 2 to 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[1]	124[2]		
Units: Liters per minute				
least squares mean (standard error)	188.77 (± 3.774)	188.31 (± 3.79)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.931
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.85
upper limit	10.76

Primary: Mean morning (AM) peak expiratory flow (PEF) on diary card over the treatment assessment period (PP Population)

End point title	Mean morning (AM) peak expiratory flow (PEF) on diary card over the treatment assessment period (PP Population)

End point description:

PEF is the maximum flow generated during a forceful exhalation, starting from full lung inflation. Par. (if needed with the help of parents or guardian) recorded on diary card the best of three PEF measurements, using a mini-Wright peak flow meter in the morning before taking any study medication. Only data that was drawn from Days 2 to 8 after randomization and on or before one day after the end date of study drug was used for analysis. The endpoint was considered missing if less than 2 days were recorded in the given treatment assessment period. Two par. from fluticasone propionate group and 5 par. from prednisone group had the missing endpoint. Analysis was performed using an analysis of covariance (ANCOVA) model with effects due to gender, age, center and treatment group. Per Protocol (PP) Population: all par. in the ITT Population who did not have any full protocol deviations.

End point type	Primary

End point timeframe:

Days 2 to 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114[3]	120[4]		
Units: Liters per minute				
least squares mean (standard error)	189.46 (± 3.724)	188.96 (± 3.712)		

Notes:

[3] - PP Population

[4] - PP Population

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	234
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.922
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.64
upper limit	10.65

Secondary: Mean evening (PM) PEF on diary card over the treatment assessment period

End point title	Mean evening (PM) PEF on diary card over the treatment assessment period

End point description:

PEF is the maximum flow generated during a forceful exhalation, starting from full lung inflation. Par. recorded on diary card the best of three PEF measurements, using a mini-Wright peak flow meter in the evening (6:00-9:00PM) before taking any study medication. Only data that was drawn from Days 1/2 to 8 after randomization and before or on the end date of study drug was used for analysis. If par. started to take the study drug in the morning (early or on 12:00 PM), only then the PM PEF on the date of randomization was used. If par. started to take the study drug in the afternoon (later than 12:00 PM), then PM PEF on the date of randomization was not used.The endpoint was considered missing if less than 2 days was recorded in the given treatment assessment period. Two par. from fluticasone propionate group and 5 par. from prednisone group had the missing endpoint. Analysis was performed using an ANCOVA model with effects due to gender, age, center and treatment group.

End point type	Secondary

End point timeframe:

Days 1/2 to 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[5]	123[6]		
Units: Liters per minute				
least squares mean (standard error)	195.79 (± 3.723)	194.63 (± 3.751)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.822
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.02
upper limit	11.34

Secondary: Median day-time and night-time symptom scores over the treatment assessment period

End point title	Median day-time and night-time symptom scores over the treatment assessment period

End point description:

The symptoms of cough, sputum production, wheeze and dyspnoea were assessed in morning and evening, and recorded on par. diary cards. Day time symptoms were scored while retiring to bed on a scale of 0 (no symptoms) to 5 (severe). Night time symptoms were scored while waking in the morning on a scale of 0 (no symptoms) to 4 (severe). For day-time score, only data that was from Days 2 to 8 after randomization and before or on the end date of study drug was used. For night-time score, only data that are from Days 2 to 8 after randomization and on or before one day after the end date of study drug was used. The endpoints were considered missing if less than 2 days were recorded in the given treatment assessment period. The analysis only includes participants with at least 2 days of non-missing symptom scores in the given treatment assessment period. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Days 2 to 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[7]	128[8]		
Units: Scores on a scale				
median (full range (min-max))				
Daytime symptom score, n=121, 123	0.5 (0 to 3)	1 (0 to 3)		
Nighttime symptom score, n=121, 124	0 (0 to 3)	0 (0 to 4)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	For median daytime symptom score
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.717
Method	Wilcoxon rank sum test

Statistical analysis title	For median night time symptom score
Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.683
Method	Wilcoxon rank sum test

Secondary: Median number of use of rescue medications during day and night over the treatment assessment period

End point title	Median number of use of rescue medications during day and night over the treatment assessment period

End point description:

The use of nebulized salbutamol (doses/puffs and frequency) were recorded on diary card in the morning and evening. The median numbers of times rescue medication during day and night was calculated for each participant over the treatment assessment period. In each case, only data that was from Days 2 to 8 after randomization and before or on the end date of study drug was used. The endpoint was considered missing if less than 2 days (that is., 24-hour periods) were recorded in the given treatment assessment period. The analysis only includes participants who have at least 2 days of non-missing numbers of times rescue medication (including zero) in the given treatment assessment period.

End point type	Secondary

End point timeframe:

Days 2 to 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[9]	123[10]		
Units: Number of use of rescue medication				
median (full range (min-max))	2 (0 to 3)	2 (0 to 3)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.996
Method	Wilcoxon rank sum test

Secondary: Clinical assessment of lung function during the treatment period

End point title	Clinical assessment of lung function during the treatment period

End point description:

Spirometric assessments of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were assessed at clinic visit 1 (Screening), 2 (Day 5) and 3 (Day 8). Lung function tests were performed at the approximately same time at each visit in the morning. Participants were instructed to withhold salbutamol therapy for at least 4 hour, and the highest of three FEV1 and FVC measurements were recorded. If participants discontinued before or on Day 5, then the FEV1 and FVC collected at the early withdrawal visit is included in the Visit 2. Otherwise, the FEV1, FVC collected at the early withdrawal visit was included in the Visit 3. Analysis was performed using ANCOVA with covariates of gender, center, age and treatment. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

During the treatment period at Day 5, Day 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[11]	128[12]		
Units: Liters				
least squares mean (standard error)				
FEV1, Day 5, n=102, 114	1.288 (± 0.0348)	1.331 (± 0.0332)		
FEV1, Day 8, n=103, 118	1.4 (± 0.0294)	1.396 (± 0.028)		
FVC, Day 5, n=107, 118	1.476 (± 0.0454)	1.543 (± 0.0439)		
FVC, Day 8, n=109, 121	1.544 (± 0.0326)	1.582 (± 0.0316)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

Statistical analysis title	FEV1, Day 5
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.348
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.044
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.135
upper limit	0.048

Statistical analysis title	FEV1, Day 8
Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.914
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.074
upper limit	0.083

Statistical analysis title	FVC, Day 5
Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.276
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.067
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.187
upper limit	0.054

Statistical analysis title	FVC, Day 8

Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.384
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.039
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.126
upper limit	0.049

Secondary: Change from Baseline in Clinical scoring index at Day 5 and Day 8

End point title	Change from Baseline in Clinical scoring index at Day 5 and Day 8

End point description:

The clinical scoring index was assessed at Baseline (Visit 1), Day 5 and Day 8. The score assigned represents the sum of the score for each of four signs: respiratory rate, wheezing, inspiration/expiration ratio, and accessory muscle use. Each of these parameters was scored from 0 to 3 where none=0, mild=1, moderate=2, severe=3. The Baseline value was the last non-missing values prior to randomisation. Change from Baseline was calculated/defined as value at the indicated visit minus value at the Baseline. If participants discontinued before or on Day 5, then the clinical scoring index collected at the early withdrawal visit was included in the Visit 2. Otherwise, the clinical scoring index collected at the early withdrawal visit was included in the Visit 3.Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline, Day 5 and Day 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[13]	128[14]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 5, n=121, 125	-2.7 (± 1.41)	-2.6 (± 1.44)		
Day 8, n=116, 123	-3.4 (± 1.26)	-3.4 (± 1.26)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

Statistical analysis title	Day 5
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.507
Method	Wilcoxon rank sum test

Statistical analysis title	Day 8
Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7
Method	Wilcoxon rank sum test

Secondary: Participant/parent and investigator global evaluation for efficacy

End point title	Participant/parent and investigator global evaluation for efficacy

End point description:

At Visit 3 (Day 8), participant/parent and investigator were asked to evaluate efficacy globally as very beneficial=1, beneficial=2, no effect=3 or worse=4. The global evaluation collected at the early withdrawal visit was included in the Visit 3. If participants were discontinued at Visit 2, then the global evaluation collected at the Visit 2 is also included in the Visit 3 for summary and analysis. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Day 8

End point values	Fluticasone propionate	Prednisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[15]	128[16]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Participant/parent global evaluation, n=122,128	1.5 (± 0.59)	1.5 (± 0.52)		
Investigator global evaluation, n=121,128	1.5 (± 0.56)	1.5 (± 0.52)		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

Statistical analysis title	Participant/parent global evaluation
Comparison groups	Fluticasone propionate v Prednisone

Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.633
Method	Wilcoxon rank sum test

Statistical analysis title	Investigator global evaluation
Comparison groups	Fluticasone propionate v Prednisone
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.323
Method	Wilcoxon rank sum test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of study medication through the treatment Phase (8 days post-dose) and assessed up to 23 days.

Adverse event reporting additional description:

Safety Population: comprised of participants randomized to treatment and who received at least one dose of study drug. Participants were assigned to the treatment group as per treatment actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Fluticasone propionate

Reporting group description:

Participants received fluticasone propionate (FP) inhalation solution twice daily 2x0.5 milligrams (mg)/milliliters (mL) via a nebulizer in morning and evening for 7 days. Participants also received placebo tablets once daily in the morning for 7 days. Salbutamol was provided on a needed basis throughout the treatment period.

Reporting group title	Prednisone

Reporting group description:

Participants received oral prednisone (Pred) tablets once daily at 2 mg per kilogram (kg) per day, up to 40 mg per day for 4 days, then 1 mg per kg per day or half of the original dose, up to 20 mg per day for 3 days in the morning. Participants also received placebo nebules 2×2mL 0.9% saline twice daily (in morning and evening) for 7 days. Salbutamol was provided on an needed basis throughout the treatment period.

Serious adverse events	Fluticasone propionate	Prednisone	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 123 (0.81%)	2 / 128 (1.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 123 (0.81%)	2 / 128 (1.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Fluticasone propionate	Prednisone	
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 123 (3.25%)	18 / 128 (14.06%)	
Investigations White blood cell count increased subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1	10 / 128 (7.81%) 10	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1	5 / 128 (3.91%) 5	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 123 (1.63%) 2	3 / 128 (2.34%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2013	Amendment 01: To amend the dosing time of the Prednisone tablets on the day of randomization

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported