Clinical trial results:
HZA106855: A dose-ranging study of fluticasone furoate (FF) inhalation powder in children aged 5-11 years with asthma.

Summary

EudraCT number	2011-003338-15
Trial protocol	SE DE Outside EU/EEA PL LV
Global end of trial date	24 September 2014

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	28 March 2015

Trial information

Trial identification

Sponsor protocol code	HZA106855

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01563029
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 Response Center, GlaxoSmithKline, 1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000431-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the dose response, efficacy and safety of three doses of fluticasone furoate (FF) inhalation powder administered once daily in the evening to children aged 5-11 years with persistent uncontrolled asthma over a 12 week treatment period.

Protection of trial subjects:

The following steps were taken to protect trial participants:
1). Only participants meeting all of the inclusion criteria and none of the exclusion criteria were randomized to investigational medication.
2). All participants enrolled into the study were provided rescue medication for use as necessary.
3). Subject lung function, as measured by morning (AM) and evening (PM) peak expiratory flow (PEF), was monitored for stability through the use of a daily electronic diary.
4). The investigator or treating physician could have unblinded a participant's treatment assignment in the case of an emergency, when knowledge of the study treatment was essential for the appropriate clinical management or welfare of the participant.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 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	Poland: 163
Country: Number of subjects enrolled	Bulgaria: 43
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Latvia: 34
Country: Number of subjects enrolled	Russian Federation: 129
Country: Number of subjects enrolled	United States: 359
Country: Number of subjects enrolled	Puerto Rico: 11
Country: Number of subjects enrolled	Japan: 135
Country: Number of subjects enrolled	Ukraine: 92
Country: Number of subjects enrolled	Peru: 163
Country: Number of subjects enrolled	Mexico: 323
Country: Number of subjects enrolled	Georgia: 24
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Philippines: 8

Country: Number of subjects enrolled	Sweden: 18
Worldwide total number of subjects	1540
EEA total number of subjects	293

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)	1540
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:

1540 participants were screened, 596 participants were randomized, and 593 participants comprise the Intent to Treat Population which include all participants who received at least one dose of study treatment. Participants were stratified at randomization according to their prior inhaled corticosteroid (ICS) use.

Pre-assignment

Screening details:

Participants who met the eligibility criteria at screening (Visit 1) entered a 4-week Run-in Period during which they continued their existing medications. Participants who met the randomization criteria (remained uncontrolled despite baseline therapy) at Visit 3 were randomized to 1 of 5 treatment arms for 12 weeks followed by a 1-week follow-up.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo once daily (OD) in the evening via a dry powder inhaler (DPI) and placebo twice daily (BID), once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

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

Dosage and administration details:

Participants received placebo once daily (OD) in the evening via a dry powder inhaler (DPI) and placebo twice daily (BID), once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Arm title	FF 25 µg OD

Arm description:

Participants received fluticasone furoate (FF) 25 micrograms (µg) OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

25 µg (micrograms) once daily via a dry powder inhaler

Arm title	FF 50 µg OD

Arm description:

Participants received FF 50 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

50 µg once daily via a dry powder inhaler

Arm title	FF 100 µg OD

Arm description:

Participants received FF 100 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

100 µg once daily via a dry powder inhaler

Arm title	FP 100 µg BID

Arm description:

Participants received fluticasone propionate (FP) 100 µg BID, once in the morning and once in the evening via a DPI and placebo OD in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Arm type	Active comparator
Investigational medicinal product name	fluticasone propionate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

100 µg twice daily via a dry powder inhaler

Number of subjects in period 1[1]	Placebo	FF 25 µg OD	FF 50 µg OD
Started	119	118	120
Completed	66	94	87
Not completed	53	24	33
Physician decision	3	5	2

Consent withdrawn by subject	4	1	3
Adverse event, non-fatal	1	-	1
Protocol defined stopping criteria	1	-	-
Lost to follow-up	1	-	1
Lack of efficacy	42	16	23
Protocol deviation	1	2	3

Number of subjects in period 1[1]	FF 100 µg OD	FP 100 µg BID
Started	118	118
Completed	85	89
Not completed	33	29
Physician decision	4	2
Consent withdrawn by subject	4	3
Adverse event, non-fatal	2	1
Protocol defined stopping criteria	-	-
Lost to follow-up	1	1
Lack of efficacy	21	19
Protocol deviation	1	3

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: 1540 participants were enrolled and screened, 596 participants were randomized, and 593 participants comprise the Intent to Treat which include all participants who received at least one dose of study treatment and is outlined in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo once daily (OD) in the evening via a dry powder inhaler (DPI) and placebo twice daily (BID), once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.	
Reporting group title	FF 25 µg OD
Reporting group description:	
Participants received fluticasone furoate (FF) 25 micrograms (µg) OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.	
Reporting group title	FF 50 µg OD
Reporting group description:	
Participants received FF 50 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.	
Reporting group title	FF 100 µg OD
Reporting group description:	
Participants received FF 100 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.	
Reporting group title	FP 100 µg BID
Reporting group description:	
Participants received fluticasone propionate (FP) 100 µg BID, once in the morning and once in the evening via a DPI and placebo OD in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.	

Reporting group values	Placebo	FF 25 µg OD	FF 50 µg OD
Number of subjects	119	118	120
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	8	7.9	8.4
standard deviation	± 1.91	± 2.08	± 1.62

Gender categorical Units: Subjects			
Female	49	41	46
Male	70	77	74
Race, Customized Units: Subjects			
African American/African Heritage	4	4	7
American Indian or Alaskan Native	24	17	16
Asian -Central/South Asian Heritage	1	0	1
Asian - Japanese Heritage	7	7	5
White - Arabic/North African Heritage	1	2	0
White - White/Caucasian/European Heritage	47	55	51
Mixed Race	35	33	40

Reporting group values	FF 100 µg OD	FP 100 µg BID	Total
Number of subjects	118	118	593
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	7.8	7.9	
standard deviation	± 2.04	± 1.87	-
Gender categorical Units: Subjects			
Female	48	39	223
Male	70	79	370
Race, Customized Units: Subjects			
African American/African Heritage	8	7	30
American Indian or Alaskan Native	17	21	95
Asian -Central/South Asian Heritage	0	0	2
Asian - Japanese Heritage	2	7	28
White - Arabic/North African Heritage	1	0	4
White - White/Caucasian/European Heritage	51	43	247
Mixed Race	39	40	187

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening via a dry powder inhaler (DPI) and placebo twice daily (BID), once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 25 µg OD

Reporting group description:

Participants received fluticasone furoate (FF) 25 micrograms (µg) OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 50 µg OD

Reporting group description:

Participants received FF 50 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 100 µg OD

Reporting group description:

Participants received FF 100 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FP 100 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 100 µg BID, once in the morning and once in the evening via a DPI and placebo OD in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Subject analysis set title	Intent to Treat Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

participants randomized to treatment who received at least 1 dose of study medication.

Subject analysis set title	Average of FF 50 µg OD and FF 100 µg OD
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All participants who received FF 100 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks and all participants who FF 50 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Primary: Change from Baseline in daily pre-dose morning (AM) peak expiratory flow (PEF) from participant electronic daily diary averaged over the 12-week Treatment Period

End point title	Change from Baseline in daily pre-dose morning (AM) peak expiratory flow (PEF) from participant electronic daily diary averaged over the 12-week Treatment Period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each morning prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. The best of three measurements was recorded. Change from Baseline was calculated as the value of the averaged daily AM PEF over the 12-week Treatment Period minus the Baseline value. The Baseline PEF value is

defined as the average of the last 7 days of the Run-in Period. Statistical analysis was performed using an analysis of covariance (ANCOVA) model with covariates of Baseline AM PEF, pre-screening inhaled corticosteroid (ICS) use, region, sex, age, and treatment. Particpants analyzed included those who have PEF data for at least 2 non-missing days in the Baseline week prior to randomisation and at least 2 non-missing days after randomisation.

End point type	Primary

End point timeframe:

Baseline, Week 1 up to Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[1]	117[2]	118[3]	118[4]
Units: Liters per minute (L/min)				
least squares mean (standard error)	3.3 (± 2.63)	21.9 (± 2.66)	22.8 (± 2.65)	15.8 (± 2.64)

Notes:

[1] - ITT Population participants randomized to treatment who received at least 1 dose of study medication
[2] - ITT Population participants randomized to treatment who received at least 1 dose of study medication
[3] - ITT Population participants randomized to treatment who received at least 1 dose of study medication
[4] - ITT Population participants randomized to treatment who received at least 1 dose of study medication

End point values	FP 100 µg BID	Average of FF 50 µg OD and FF 100 µg OD		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	117[5]	236[6]		
Units: Liters per minute (L/min)				
least squares mean (standard error)	17.3 (± 2.64)	19.3 (± 1.86)		

Notes:

[5] - ITT Population participants randomized to treatment who received at least 1 dose of study medication
[6] - ITT Population participants randomized to treatment who received at least 1 dose of study medication

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Gate-keeper analysis

Comparison groups	Placebo v Average of FF 50 µg OD and FF 100 µg OD
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	16

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.6
upper limit	22.4

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Inference for FF 100 µg versus (vs) placebo and FF 50 ug versus placebo was dependent upon statistical significance (SS) having first been achieved for the average of the higher two doses of FF (FF 100 ug and 50 ug) versus placebo comparison.

Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.1
upper limit	19.8

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Inference for FF 100 µg versus (vs) placebo and FF 50 ug versus placebo was dependent upon statistical significance (SS) having first been achieved for the average of the higher two doses of FF (FF 100 ug and 50 ug) versus placebo comparsion.

Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.1
upper limit	26.9

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Inference for FF 25 ug versus placebo was dependent upon statistical significance (SS) having first been achieved for both the FF 100 ug versus placebo comparison and the FF 50 ug versus placebo comparison.

Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.3
upper limit	26

Statistical analysis title	Statistical analysis 5
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	14
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	21.4

Secondary: Change from Baseline in evening clinic visit trough (pre-bronchodilator and pre-dose) forced expiratory volume in one second (FEV1) at the end of the 12-week Treatment Period in children who could perform the maneuver

End point title	Change from Baseline in evening clinic visit trough (pre-bronchodilator and pre-dose) forced expiratory volume in one second (FEV1) at the end of the 12-week Treatment Period in children who could perform the maneuver

End point description:

Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 is defined as a pre-dose FEV1 measurement taken at a clinic visit while still on treatment. Change from Baseline was calculated as the Week 12 trough FEV1 value minus the Baseline value. The Baseline FEV1 value is defined as the value at Visit 3 (randomization). The analysis was performed using an ANCOVA model with covariates of Baseline trough FEV1, region, actual pre-screening ICS use, sex, age, and treatment. The last observation carried forward (LOCF) method was used to impute missing data, in which the last non-missing post-Baseline on-treatment measurement at scheduled clinic visits was used to impute the missing measurements. Only those participants available at the specified time points were analyzed.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	102[7]	96[8]	112[9]	96[10]
Units: Liters				
least squares mean (standard error)	0.128 (± 0.0264)	0.254 (± 0.0272)	0.15 (± 0.0252)	0.162 (± 0.0272)

Notes:

[7] - ITT Population, only participants available at the specified time points were analyzed.

[8] - ITT Population, only participants available at the specified time points were analyzed.

[9] - ITT Population, only participants available at the specified time points were analyzed.

[10] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	102[11]			
Units: Liters				
least squares mean (standard error)	0.192 (± 0.0262)			

Notes:

[11] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.126
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.051
upper limit	0.201

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD

Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.551
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.094

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.379
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.041
upper limit	0.108

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.089
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.064
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.137

Secondary: Change from Baseline in the percentage of rescue-free 24-hour periods

during the 12-week Treatment Period	
End point title	Change from Baseline in the percentage of rescue-free 24-hour periods during the 12-week Treatment Period

End point description:

The number of inhalations of rescue albuterol/salbutamol aerosol (medication used to relieve symptoms immediately) used during the day and night) was recorded by the participants in a daily diary. A 24-hour (hr) period in which a participant's responses to both the morning and evening assessments indicated no use of rescue medication was considered as rescue free. Participants who were rescue free for 24-hour periods during the 12-week Treatment Period were assessed. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant. Change from Baseline was calculated as the average value during the 12-week Treatment Period minus the value at Baseline. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, actual pre-screening ICS use, age, and treatment.

End point type	Secondary

End point timeframe:

Baseline, Week 1 up to Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[12]	117[13]	118[14]	118[15]
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	16.5 (± 3.01)	24.9 (± 3.03)	26.3 (± 3.03)	28.7 (± 3.02)

Notes:

[12] - ITT Population, only participants available at the specified time points were analyzed.

[13] - ITT Population, only participants available at the specified time points were analyzed.

[14] - ITT Population, only participants available at the specified time points were analyzed.

[15] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	117[16]			
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	22.7 (± 3.01)			

Notes:

[16] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	16.9

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	18.2

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	20.5

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID

Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.143
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	14.6

Secondary: Change from Baseline in daily evening (PM) PEF averaged over the 12-week Treatment Period

End point title	Change from Baseline in daily evening (PM) PEF averaged over the 12-week Treatment Period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. Change from Baseline was calculated as the value of the averaged daily PM PEF over the 12-week Treatment Period (at Week 12) minus the Baseline value. The Baseline PEF value is defined as the average of the last 7 days of the Run-in Period. Statistical analysis was performed using ANCOVA model with covariates of Baseline, pre-screening ICS use, region, sex, age, and treatment. Particpants analyzed included those who have PEF data for at least 2 non-missing days in the Baseline week prior to randomisation and at least 2 non-missing days after randomisation.

End point type	Secondary

End point timeframe:

Baseline, Week 1 up to Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[17]	117[18]	119[19]	118[20]
Units: liters per minute (L/min)				
least squares mean (standard error)	5.1 (± 2.76)	16.3 (± 2.81)	18.5 (± 2.77)	13.5 (± 2.78)

Notes:

[17] - ITT Population, only participants available at the specified time points were analyzed.

[18] - ITT Population, only participants available at the specified time points were analyzed.

[19] - ITT Population, only participants available at the specified time points were analyzed.

[20] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	117[21]			
Units: liters per minute (L/min)				
least squares mean (standard error)	13.1 (± 2.77)			

Notes:
[21] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	19

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	21.1

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD

Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	16.1

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.042
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	15.7

Secondary: Change from Baseline in PM PEF over the last 7 days of the Treatment Period (Week 12)

End point title	Change from Baseline in PM PEF over the last 7 days of the Treatment Period (Week 12)

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. Change from Baseline in PM PEF was calculated as the value over the last 7 days of the Treatment Period minus the Baseline value. The Baseline PEF value is defined as the average of the last 7 days of the Run-in Period. Statistical analysis was performed using ANCOVA model with covariates of Baseline, actual pre-screening ICS use, region, sex, age, and treatment. The LOCF method was used to impute missing data, in which the last non-missing post-Baseline on-treatment measurement was used to impute the missing measurements.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[22]	117[23]	118[24]	118[25]
Units: L/min				
least squares mean (standard error)	5 (± 3.75)	16.2 (± 3.8)	18.2 (± 3.77)	11 (± 3.76)

Notes:

[22] - ITT Population, only participants available at the specified time points were analyzed.

[23] - ITT Population, only participants available at the specified time points were analyzed.

[24] - ITT Population, only participants available at the specified time points were analyzed.

[25] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	117[26]			
Units: L/min				
least squares mean (standard error)	11.3 (± 3.75)			

Notes:

[26] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.037
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	21.7

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.014
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	13.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	23.6

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.266
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	16.3

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.242
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	16.6

Secondary: Change from Baseline in AM PEF over the last 7 days of the Treatment Period (Week 12)

End point title	Change from Baseline in AM PEF over the last 7 days of the Treatment Period (Week 12)

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. Change from Baseline in AM PEF was calculated as the value over the last 7 days of the Treatment Period minus

the Baseline value. The Baseline PEF value is defined as the average of the last 7 days of the Run-in Period. Statistical analysis was performed using ANCOVA model with covariates of Baseline, pre-screening ICS use, region, sex, age, and treatment. The LOCF method was used to impute missing data, in which the last non-missing post-Baseline on-treatment measurement was used to impute the missing measurements.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[27]	117[28]	118[29]	118[30]
Units: L/min				
least squares mean (standard error)	2.7 (± 3.81)	23.3 (± 3.85)	20.6 (± 3.83)	14.2 (± 3.82)

Notes:

[27] - ITT Population, only participants available at the specified time points were analyzed.

[28] - ITT Population, only participants available at the specified time points were analyzed.

[29] - ITT Population, only participants available at the specified time points were analyzed.

[30] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	117[31]			
Units: L/min				
least squares mean (standard error)	19.3 (± 3.82)			

Notes:

[31] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	20.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	31.3

Statistical analysis title	Statistical Analysis 2

Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	17.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.2
upper limit	28.6

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.033
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	22.1

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	27.3

Secondary: Change from Baseline in the percentage of symptom-free 24-hour periods during the 12-week Treatment Period

End point title	Change from Baseline in the percentage of symptom-free 24-hour periods during the 12-week Treatment Period

End point description:

Asthma symptoms were recorded in a daily eDairy by the participants every day in the morning and evening before taking any rescue or study medication and before the PEF measurement. A 24-hour (hr) period in which a participant's responses to both the morning and evening assessments indicated no symptoms was considered to be symptom free. The Baseline symptom-free value is defined as the value at Visit 3 (randomization). Change from Baseline was calculated as the averaged value during the 12-week Treatment Period minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline, region, sex, actual pre-screening ICS use, age, and treatment group.

End point type	Secondary

End point timeframe:

Baseline, Week 1 up to Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[32]	117[33]	119[34]	118[35]
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	19 (± 2.9)	21 (± 2.92)	24.7 (± 2.9)	22.9 (± 2.91)

Notes:

[32] - ITT Population, only participants available at the specified time points were analyzed.

[33] - ITT Population, only participants available at the specified time points were analyzed.

[34] - ITT Population, only participants available at the specified time points were analyzed.

[35] - ITT Population, only participants available at the specified time points were analyzed.

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	117[36]			
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	22 (± 2.91)			

Notes:

[36] - ITT Population, only participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.619
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	10.2

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.161
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	13.9

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.34
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	12

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID

Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.459
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	11.1

Secondary: Number of withdrawals due to lack of efficacy throughout the 12-week Treatment Period

End point title	Number of withdrawals due to lack of efficacy throughout the 12-week Treatment Period

End point description:

The number of participants whose primary reason for withdrawal from the study was due to lack of efficacy is presented together with p-values for the treatment comparisons.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	FF 25 µg OD	FF 50 µg OD	FF 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119[37]	118[38]	120[39]	118[40]
Units: Participants				
number (not applicable)	42	16	23	21

Notes:

[37] - ITT Population

[38] - ITT Population

[39] - ITT Population

[40] - ITT Population

End point values	FP 100 µg BID			
Subject group type	Reporting group			
Number of subjects analysed	118[41]			
Units: Participants				
number (not applicable)	19			

Notes:

[41] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FF 25 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FF 50 µg OD
Number of subjects included in analysis	239
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.006
Method	Fisher exact

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Fisher exact

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact

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 the start of study medication until the follow-up visit (up to 13 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for members of the ITT Population, comprised of all participants who were randomized to treatment and received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening via a dry powder inhaler (DPI) and placebo twice daily (BID), once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 25 µg OD

Reporting group description:

Participants received fluticasone furoate (FF) 25 micrograms (µg) OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 50 µg OD

Reporting group description:

Participants received FF 50 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FF 100 µg OD

Reporting group description:

Participants received FF 100 µg OD in the evening via a DPI and placebo BID, once in the morning and once in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Reporting group title	FP 100 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 100 µg BID, once in the morning and once in the evening via a DPI and placebo OD in the evening via a separate DPI for 12 weeks. Participants were also provided albuterol/salbutamol inhalation aerosol via metered dose inhaler (MDI) to be used as rescue medication as determined by the investigator.

Serious adverse events	Placebo	FF 25 µg OD	FF 50 µg OD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 119 (0.00%)	0 / 118 (0.00%)	1 / 120 (0.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 119 (0.00%)	0 / 118 (0.00%)	1 / 120 (0.83%)
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			
Hepatitis A			
subjects affected / exposed	0 / 119 (0.00%)	0 / 118 (0.00%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	FF 100 µg OD	FP 100 µg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 118 (0.85%)	0 / 118 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 118 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Hepatitis A			
subjects affected / exposed	1 / 118 (0.85%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	FF 25 µg OD	FF 50 µg OD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 119 (16.81%)	27 / 118 (22.88%)	20 / 120 (16.67%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 119 (0.00%)	3 / 118 (2.54%)	0 / 120 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 119 (1.68%)	2 / 118 (1.69%)	2 / 120 (1.67%)
occurrences (all)	2	2	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 119 (0.00%)	4 / 118 (3.39%)	1 / 120 (0.83%)
occurrences (all)	0	4	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 119 (5.04%)	7 / 118 (5.93%)	1 / 120 (0.83%)
occurrences (all)	8	9	1
Rhinorrhoea			
subjects affected / exposed	2 / 119 (1.68%)	6 / 118 (5.08%)	1 / 120 (0.83%)
occurrences (all)	2	9	1
Oropharyngeal pain			
subjects affected / exposed	1 / 119 (0.84%)	6 / 118 (5.08%)	2 / 120 (1.67%)
occurrences (all)	1	8	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 119 (3.36%)	9 / 118 (7.63%)	4 / 120 (3.33%)
occurrences (all)	5	12	5
Pharyngitis			
subjects affected / exposed	4 / 119 (3.36%)	2 / 118 (1.69%)	7 / 120 (5.83%)
occurrences (all)	5	2	8
Bronchitis			
subjects affected / exposed	1 / 119 (0.84%)	2 / 118 (1.69%)	4 / 120 (3.33%)
occurrences (all)	1	2	4
Upper respiratory tract infection			
subjects affected / exposed	3 / 119 (2.52%)	1 / 118 (0.85%)	0 / 120 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	FF 100 µg OD	FP 100 µg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 118 (24.58%)	24 / 118 (20.34%)	
Investigations			

Body temperature increased			
subjects affected / exposed	0 / 118 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	4	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 118 (5.93%)	4 / 118 (3.39%)	
occurrences (all)	10	10	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 118 (1.69%)	1 / 118 (0.85%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 118 (8.47%)	5 / 118 (4.24%)	
occurrences (all)	12	5	
Rhinorrhoea			
subjects affected / exposed	6 / 118 (5.08%)	5 / 118 (4.24%)	
occurrences (all)	8	5	
Oropharyngeal pain			
subjects affected / exposed	2 / 118 (1.69%)	4 / 118 (3.39%)	
occurrences (all)	2	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 118 (2.54%)	4 / 118 (3.39%)	
occurrences (all)	3	4	
Pharyngitis			
subjects affected / exposed	5 / 118 (4.24%)	1 / 118 (0.85%)	
occurrences (all)	5	2	
Bronchitis			
subjects affected / exposed	2 / 118 (1.69%)	2 / 118 (1.69%)	
occurrences (all)	2	2	
Upper respiratory tract infection			
subjects affected / exposed	4 / 118 (3.39%)	3 / 118 (2.54%)	
occurrences (all)	4	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 February 2012	The purpose of this amendment is to specify that Japan will not conduct the Paediatric Asthma Quality of Life (PAQLQ) measure on children enrolled in this protocol.
05 July 2012	The purpose of this amendment is to make changes to the ICS doses allowed prior to Visit 1. Additional edits were made to the statistical sections to the effect that the primary analysis will be the comparison of each dose regimen of fluticasone furoate with placebo.
14 December 2012	The purpose of this amendment is to revise the dose for Clenil and Qvar used prior to Visit 1 and to allow for the-re screening of subjects who failed Visit 1 criteria.
19 September 2013	The purpose of this amendment is to implement a change to the time of the primary endpoint, daily PEF, from evening to morning assessments. Additional edits were made to the time point for the primary endpoint (from an endpoint assessment to the average over the treatment period) and to the statistical analysis of the primary endpoint including multiplicity adjustment methods.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported