Clinical trial results:
A randomised, double-blind, double-dummy, parallel group study to evaluate the efficacy and safety of flutica one furoate /vil nterol trifenatate (FF/VI) inhalation powder delivered once daily compared to fluticasone propionate delivered twice daily in the treatment of asthma in adolescent and adult subjects of Asian ancestry currently treated with high-strength inhaled corticosteroids or mid-strength IC S/LABA combination therapy.

Summary

EudraCT number	2015-004868-11
Trial protocol	Outside EU/EEA
Global end of trial date	01 February 2013

Results information

Result version number	v1 (current)
This version publication date	20 January 2017
First version publication date	20 January 2017

Trial information

Trial identification

Sponsor protocol code	113714

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 Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	09 April 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

TBD

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 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: 200
Country: Number of subjects enrolled	Korea, Republic of: 59
Country: Number of subjects enrolled	Philippines: 50
Worldwide total number of subjects	309
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)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	276
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 313 participants were randomized to treatment. However, 4 participants were randomized in error and did not receive any study treatment; thus, these participants were not included in the Intent-to-Treat (ITT) Population, comprised of all participants randomized to treatment who received >=1 dose of trial medication.

Pre-assignment

Screening details:

At screening, participants who meet all of the inclusion criteria entered a 2-week Run-in period. Participants continued on inhaled corticosteroid (ICS) therapy throughout the Run-in period. At the end of the Run-in period, participants meeting the randomization criteria entered a 12-week Treatment Period and received one of the two treatments.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Fluticasone furoate/vilanterol 200/25 µg once daily

Arm description:

Participants received fluticasone furoate (FF)/vilanterol (VI) 200/25 micrograms (µg) once daily (OD) in the evening,via a Dry Powder Inhaler (DPI), for a period of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Furoate/Vilanterol (FF/VI) Trifenatate (200/25 mcg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Administered once daily in the evening by using a Novel Dry Powder Inhaler (NDPI)

Arm title	Fluticasone propionate 500 µg twice daily (BID)

Arm description:

Participants received fluticasone propionate (FP) 500 µg inhalation powder BID (in the morning and evening), via the DISKUS, for a period of 12 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fluticasone propionate (500 mcg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

administered twice daily via DISKUS Inhaler

Number of subjects in period 1	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)
Started	155	154
Completed	136	119
Not completed	19	35
Physician decision	2	-
Consent withdrawn by subject	2	3
Adverse event, non-fatal	2	2
Lost to follow-up	1	-
Lack of efficacy	12	26
Protocol deviation	-	4

Baseline characteristics

Reporting groups	
Reporting group title	Fluticasone furoate/vilanterol 200/25 µg once daily
Reporting group description:	
Participants received fluticasone furoate (FF)/vilanterol (VI) 200/25 micrograms (µg) once daily (OD) in the evening,via a Dry Powder Inhaler (DPI), for a period of 12 weeks.	
Reporting group title	Fluticasone propionate 500 µg twice daily (BID)
Reporting group description:	
Participants received fluticasone propionate (FP) 500 µg inhalation powder BID (in the morning and evening), via the DISKUS, for a period of 12 weeks.	

Reporting group values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)	Total
Number of subjects	155	154	309
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	46.9	48.8	
standard deviation	± 12.93	± 13.41	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	96	86	182
Male	59	68	127
Race/Ethnicity, Customized Units: Subjects			
Asian - East Asian Heritage	128	127	255
Asian - South East Asian Heritage	27	27	54

End points

End points reporting groups

Reporting group title	Fluticasone furoate/vilanterol 200/25 µg once daily
Reporting group description:	
Participants received fluticasone furoate (FF)/vilanterol (VI) 200/25 micrograms (µg) once daily (OD) in the evening,via a Dry Powder Inhaler (DPI), for a period of 12 weeks.	
Reporting group title	Fluticasone propionate 500 µg twice daily (BID)
Reporting group description:	
Participants received fluticasone propionate (FP) 500 µg inhalation powder BID (in the morning and evening), via the DISKUS, for a period of 12 weeks.	

Primary: Mean change from Baseline (BL) in daily evening (PM) peak expiratory flow (PEF) averaged over the 12-week Treatment Period

End point title	Mean change from Baseline (BL) in daily evening (PM) peak expiratory flow (PEF) averaged over the 12-week Treatment Period
End point description:	
Peak Expiratory Flow is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. 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 value of the averaged daily PM PEF over the 12-week Treatment Period minus the Baseline value. Analysis was performed using Analysis of Covariance (ANCOVA) with covariates of Baseline, region, sex, age, and treatment. Intent-to-Treat (ITT) Population: all participants randomized to treatment who received >=1 dose of trial medication. The primary endpoint analysis only included participants who had PM PEF data for >=4 days in the BL week prior to randomization and >=4 days after randomization. Only participants available at the indicated time point were assessed.	
End point type	Primary
End point timeframe:	
Baseline and Weeks 1-12 (up to Day 84)	

End point values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154[1]	152[2]		
Units: Liters/minute (L/min)				
least squares mean (standard error)	39.1 (± 3.01)	10.5 (± 3.03)		

Notes:

[1] - Intent-to-Treat (ITT) Population

[2] - Intent-to-Treat (ITT) Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Fluticasone propionate 500 µg twice daily (BID) v Fluticasone furoate/vilanterol 200/25 µg once daily

Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	28.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.1
upper limit	36.9

Secondary: Mean change from Baseline in daily morning (AM) PEF averaged over the 12-week Treatment Period

End point title	Mean change from Baseline in daily morning (AM) 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. 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 value of the averaged daily AM PEF over the 12-week Treatment Period minus the Baseline value. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment. ITT Population. In addition, the analysis only included participants who had PM PEF data for at least 2 days in the Baseline week prior to randomization and at least 2 days after randomization. Only those participants available at the indicated time point were assessed.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12 (up to Day 84)

End point values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154[3]	152[4]		
Units: L/min				
least squares mean (standard error)	46.2 (± 3.07)	14 (± 3.1)		

Notes:

[3] - ITT Population

[4] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the percentage of rescue-free 24-hour (hr) periods during the 12-week Treatment Period

End point title	Mean change from Baseline in the percentage of rescue-free 24-hour (hr) periods during the 12-week Treatment Period

End point description:

Number of inhalations of rescue albuterol/salbutamol inhalation aerosol used during the day and night was recorded by the participants (Par.) in a daily diary. A 24-hour period in which a par. responses to both the morning and evening assessments indicated no use of rescue medication was considered as rescue free. Par. (who were rescue free for 24-hour periods during the 12-week Treatment Period were assessed. Baseline value was derived from the last 7 days of the daily diary prior to the randomization (ran.) of the par. Change from Baseline is 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, age, and treatment. ITT Population.In addition, analysis only included par. who had rescue-free 24-hour period data for at least 2 days in the Baseline week prior to ran. and at least 2 days after ran. Only those par. available at the indicated time point were assessed.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12 (up to Day 84)

End point values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155[5]	152[6]		
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	32.4 (± 2.95)	31.5 (± 2.98)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week Treatment Period

End point title	Mean change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week Treatment Period

End point description:

Asthma symptoms were recorded in a daily dairy by the participants (Par) every day in the morning and evening before taking any rescue or study medication and before PEF measurement. A 24-hour period in which a par. responses to both the morning and evening assessments indicated no symptoms was considered as symptom free. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the par.. Par. who were symptom free for 24-hour periods during the 12-week Treatment Period were assessed. Change from Baseline is 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, age, and treatment. ITT Population. In addition, the analysis only included par. who had symptom-free 24-hour period data for at least 2 days in the Baseline week prior to randomization and at least 2 days after randomization. Only those par. assessed.

End point type	Secondary

End point timeframe:

Baseline and Weeks 1-12 (up to Day 84)

End point values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155[7]	152[8]		
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	25.4 (± 2.74)	20.6 (± 2.77)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total Asthma Quality of Life Questionnaire (AQLQ) score at Week 12

End point title	Change from Baseline in total Asthma Quality of Life Questionnaire (AQLQ) score at Week 12

End point description:

The AQLQ is a disease-specific, self-administered quality of life questionnaire developed to evaluate the impact of asthma treatments on the quality of life of asthma sufferers. The AQLQ contains 32 items in 4 domains: activity limitation (11 items), symptoms (12 items), emotional function (5 items), and environmental stimuli (4 items). The 32 items of the questionnaire are averaged to produce one overall quality of life score. The response format consists of a 7-point scale, where a value of 1 indicates "total impairment" and a value of 7 indicates "no impairment." Change from Baseline was calculated as the Week 12 value minus the Baseline value. Analysis was performed using ANCOVA with covariates of Baseline, region, sex, age, and treatment. ITT Population. Only those participants available at the indicated time point were assessed.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Fluticasone furoate/vilanterol 200/25 µg once daily	Fluticasone propionate 500 µg twice daily (BID)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140[9]	123[10]		
Units: Scores on a scale				
least squares mean (standard error)	0.8 (± 0.069)	0.69 (± 0.074)		

Notes:

[9] - ITT Population. Only those participants available at the indicated time point were assessed.

[10] - ITT Population. Only those participants available at the indicated time point were assessed.

Statistical analyses

No statistical analyses for this end point

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 end of treatment (up to Study Day 84).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the Intent-to-Treat (ITT) Population, comprised of all participants randomized to treatment who received >=1 dose of trial medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Fluticasone propionate 500 µg twice daily (BID)

Reporting group description:

Participants received fluticasone propionate (FP) 500 µg inhalation powder BID (in the morning and evening), via the DISKUS, for a period of 12 weeks.

Reporting group title	Fluticasone furoate/vilanterol 200/25 µg once daily

Reporting group description:

Participants received fluticasone furoate (FF)/vilanterol (VI) 200/25 micrograms (µg) once daily (OD) in the evening, via a Dry Powder Inhaler (DPI), for a period of 12 weeks.

Serious adverse events	Fluticasone propionate 500 µg twice daily (BID)	Fluticasone furoate/vilanterol 200/25 µg once daily	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 154 (1.30%)	1 / 155 (0.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 154 (0.65%)	1 / 155 (0.65%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 154 (0.65%)	0 / 155 (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	Fluticasone propionate 500 µg twice daily (BID)	Fluticasone furoate/vilanterol 200/25 µg once daily	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 154 (16.88%)	23 / 155 (14.84%)	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	2 / 154 (1.30%)	5 / 155 (3.23%)	
occurrences (all)	3	5	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 154 (11.69%)	13 / 155 (8.39%)	
occurrences (all)	21	16	
Nasopharyngitis			
subjects affected / exposed	6 / 154 (3.90%)	6 / 155 (3.87%)	
occurrences (all)	7	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported