Clinical trial results:
12-week study with GW685698/GW642444 in Asthma (low dose) Centralised D2014-0774

Summary

EudraCT number	2015-004871-59
Trial protocol	Outside EU/EEA
Global end of trial date	16 July 2013

Results information

Result version number	v1 (current)
This version publication date	12 February 2017
First version publication date	12 February 2017

Trial information

Trial identification

Sponsor protocol code	113719

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	22 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 July 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	18 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: 360
Country: Number of subjects enrolled	Korea, Republic of: 124
Country: Number of subjects enrolled	Philippines: 78
Worldwide total number of subjects	562
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)	10
Adults (18-64 years)	497
From 65 to 84 years	54
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 311 participants were randomized to treatment. However, 4 participants were randomized in error and did not receive any study treatment. These participants were not included in the Intent-to-Treat (ITT) Population, which was comprised of all participants randomized to treatment who received >=1 dose of trial medication.

Pre-assignment

Screening details:

At screening, participants who met 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	Placebo

Arm description:

Participants received placebo once daily (OD) in the evening,via a Dry Powder Inhaler (DPI), for a period of 12 weeks.

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 in the evening, via a novel dry powder inhaler, for a period of 12 weeks.

Arm title	Fluticasone furoate/vilanterol 100/25 µg once daily

Arm description:

Participants received fluticasone furoate (FF)/vilanterol (VI) 100/25 micrograms (µg) OD in the evening,via a DPI, for a period of 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Furoate (FF)/Vilanterol Trifenatate (VI) 100/25 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received FF/VI 100/25 µg once daily in the evening, via a novel dry powder inhaler, for a period of 12 weeks

Number of subjects in period 1[1]	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily
Started	154	153
Completed	65	131
Not completed	89	22
Consent withdrawn by subject	12	4
Physician decision	-	2
Adverse event, non-fatal	1	4
Lack of efficacy	72	12
Protocol deviation	4	-

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 562 participants were screened for this study, 178 subjects were withdrawn at Screening Visit and additional 73 subjects were withdrawn during the run-in period. 311 participants were randomized to treatment; however, 4 participants were randomized in error and did not receive any study treatment.

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), for a period of 12 weeks.	
Reporting group title	Fluticasone furoate/vilanterol 100/25 µg once daily
Reporting group description:	
Participants received fluticasone furoate (FF)/vilanterol (VI) 100/25 micrograms (µg) OD in the evening,via a DPI, for a period of 12 weeks.	

Reporting group values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily	Total
Number of subjects	154	153	307
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years arithmetic mean standard deviation	 47.4 ± 13.9	 47 ± 14.01	 -
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	88	83	171
Male	66	70	136
Race/Ethnicity, Customized Units: Subjects			
Asian - East Asian Heritage	132	125	257
Asian - South East Asian Heritage	22	28	50

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), for a period of 12 weeks.	
Reporting group title	Fluticasone furoate/vilanterol 100/25 µg once daily
Reporting group description:	
Participants received fluticasone furoate (FF)/vilanterol (VI) 100/25 micrograms (µg) OD in the evening,via a DPI, 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.	
End point type	Primary
End point timeframe:	
Baseline and Weeks 1-12 (up to Day 84)	

End point values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	153		
Units: Liters/minute (L/min)				
least squares mean (standard error)	-11.8 (± 3.16)	39.2 (± 3.14)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Fluticasone furoate/vilanterol 100/25 µg once daily v Placebo
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean Difference
Point estimate	51

Confidence interval	
level	95 %
sides	2-sided
lower limit	42.2
upper limit	59.7

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. A Repeated Measures analysis adjusted for Baseline, region, sex, age, treatment, week, week by Baseline interaction, and week by treatment interaction was used.

End point type	Secondary

End point timeframe:

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

End point values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	153		
Units: L/min				
least squares mean (standard error)	-9.3 (± 3.12)	43.6 (± 3.12)		

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:

The number of inhalations of rescue albuterol/salbutamol inhalation 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 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 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.

End point type	Secondary

End point timeframe:

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

End point values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	8.3 (± 2.59)	30.1 (± 2.6)		

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 diary by the participants 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 participant's 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 participant. Participants 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.

End point type	Secondary

End point timeframe:

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

End point values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	9 (± 2.3)	24.8 (± 2.31)		

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.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	135		
Units: Scores on a scale				
least squares mean (standard error)	0.33 (± 0.094)	0.84 (± 0.068)		

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 follow up (up to Study Day 91).

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	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo OD in the evening,via a DPI, for a period of 12 weeks.

Reporting group title	Fluticasone furoate/vilanterol 100/25 µg once daily

Reporting group description:

Participants received FF/VI 100/25 µg OD in the evening,via a DPI, for a period of 12 weeks.

Serious adverse events	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 154 (0.00%)	2 / 153 (1.31%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 154 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 154 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Fluticasone furoate/vilanterol 100/25 µg once daily	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 154 (17.53%)	24 / 153 (15.69%)	
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 154 (1.95%)	7 / 153 (4.58%)	
occurrences (all)	3	18	
Infections and infestations			
Upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	14 / 154 (9.09%)	11 / 153 (7.19%)	
occurrences (all)	15	11	
Nasopharyngitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	13 / 154 (8.44%)	7 / 153 (4.58%)	
occurrences (all)	14	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