Clinical trial results:
A Randomized, Double-Blind, Parallel Group study of ADVAIR™ DISKUS™ 100/50 and FLOVENT™DISKUS™ 100, both twice daily, in a Pediatric Population during the Fall Viral Season.

Summary

EudraCT number	2015-004887-13
Trial protocol	Outside EU/EEA
Global end of trial date	16 December 2010

Results information

Result version number	v1 (current)
This version publication date	25 January 2017
First version publication date	25 January 2017

Trial information

Trial identification

Sponsor protocol code	113872

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	13 April 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2010
Global end of trial reached?	Yes
Global end of trial date	16 December 2010
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	02 August 2010
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	United States: 339
Worldwide total number of subjects	339
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)	339
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: -

Pre-assignment

Screening details:

A total of 339 participants were treated. Two hundred and ninety-two participants completed the 16-week study and 47 withdrew.

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	FSC DISKUS 100/50 mcg BID

Arm description:

Fluticasone Propionate/Salmeterol DISKUS Combination Product (FSC) at a dose of 100/50 micrograms (mcg) administered as one inhalation twice daily (BID) for 16 weeks

Arm type	Experimental
Investigational medicinal product name	Fluticasone propionate + salmeterol combination (FSC) 100/50 mcg DISKUS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

FSC was administered at a dose of 100/50 mcg as one inhalation twice daily (BID) for 16 weeks

Arm title	FP DISKUS 100 mcg BID

Arm description:

Fluticasone Propionate (FP) DISKUS 100 mcg administered as one inhalation BID for 16 weeks

Arm type	Active comparator
Investigational medicinal product name	Fluticasone propionate (FP) 100mcg DISKUS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

FP 100 mcg was administered as one inhalation BID for 16 weeks

Number of subjects in period 1	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID
Started	171	168
Completed	147	145
Not completed	24	23
Consent withdrawn by subject	6	10
Physician decision	2	4
Adverse event, non-fatal	2	1
Lost to follow-up	3	3
Protocol deviation	10	3
Lack of efficacy	1	2

Baseline characteristics

Reporting groups	
Reporting group title	FSC DISKUS 100/50 mcg BID
Reporting group description:	
Fluticasone Propionate/Salmeterol DISKUS Combination Product (FSC) at a dose of 100/50 micrograms (mcg) administered as one inhalation twice daily (BID) for 16 weeks	
Reporting group title	FP DISKUS 100 mcg BID
Reporting group description:	
Fluticasone Propionate (FP) DISKUS 100 mcg administered as one inhalation BID for 16 weeks	

Reporting group values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID	Total
Number of subjects	171	168	339
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	7.5	7.4	
standard deviation	± 2.11	± 2.08	-
Gender categorical Units: Subjects			
Female	63	56	119
Male	108	112	220
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	27	33	60
American Indian or Alaska Native	2	0	2
Asian	8	6	14
American Indian or Alaska Native and White	1	0	1
White	129	127	256
African American/African Heritage and White	1	1	2
Asian & Native Hawaiian or Other Pacific Islander	1	0	1
Asian and White	2	0	2
Native Hawaiian or Other Pacific Islander & White	0	1	1

End points

End points reporting groups

Reporting group title	FSC DISKUS 100/50 mcg BID
Reporting group description:	
Fluticasone Propionate/Salmeterol DISKUS Combination Product (FSC) at a dose of 100/50 micrograms (mcg) administered as one inhalation twice daily (BID) for 16 weeks	
Reporting group title	FP DISKUS 100 mcg BID
Reporting group description:	
Fluticasone Propionate (FP) DISKUS 100 mcg administered as one inhalation BID for 16 weeks	

Primary: Total number of asthma exacerbations reported during the treatment period

End point title	Total number of asthma exacerbations reported during the treatment period
End point description:	
An asthma exacerbation was defined as deterioration of asthma that required the use of outpatient oral/parenteral corticosteroids (tablets, suspensions, or injection) or an urgent care, hospitalization, or emergency room (ER) visit due to asthma that required oral/parenteral corticosteroids. Two exacerbations (out of a total of 51) were excluded: (1) one exacerbation occurred within 7 days of the resolution of an earlier one, and, per protocol, was combined with the previous exacerbation; and (2) one exacerbation occurred post treatment. Intent-to-Treat (ITT) Population: all participants randomized to treatment. Only those participants who reported >=1 exacerbation were analyzed.	
End point type	Primary
End point timeframe:	
From Baseline (Week 1) until the end of treatment (up to Week 16)	

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[1]	20[2]		
Units: Number of asthma exacerbations	24	25		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The risk of having an asthma exacerbation during the treatment period was analyzed.	
Comparison groups	FP DISKUS 100 mcg BID v FSC DISKUS 100/50 mcg BID

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.928 [3]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.971
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.519
upper limit	1.819

Notes:

[3] - Cox Proportional Hazards model adjusted for investigative center

Secondary: Mean asthma symptom scores, as an indicator of severity, associated with the presence of moderate or severe upper respiratory tract symptoms (URTS) or a confirmed rhinovirus (RV) infection at Baseline and during the Peak Viral Period

End point title	Mean asthma symptom scores, as an indicator of severity, associated with the presence of moderate or severe upper respiratory tract symptoms (URTS) or a confirmed rhinovirus (RV) infection at Baseline and during the Peak Viral Period

End point description:

Participants recorded their asthma symptom score over the previous 24 hours (during the day and the previous night) using the following 6-point scale: 0=No symptoms; 1=Symptoms for 1 short period; 2=Symptoms for >=2 short periods; 3=Symptoms for most of the day/previous night that did not affect normal daily activities; 4=Symptoms for most of the day/previous night that affected normal daily activities; 5=Symptoms so severe that participant could not perform normal daily activities. The Baseline mean asthma symptom score was calculated as the average score over 7 days prior to Week 1, Visit 2.

ITT Population. Only those participants with moderate or severe URTS or a confirmed RV infection were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 1) and Peak Viral Period ([period during which the greatest number of viral infections is expected] from 30 August 2010 through the end of the treatment period [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106[4]	104[5]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=105, 104	0.2 (± 0.41)	0.2 (± 0.39)		
Peak Viral Period, n=106, 104	0.5 (± 0.84)	0.4 (± 0.7)		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean duration of worsening asthma symptoms associated with the presence of moderate or severe URTS or a confirmed RV infection

End point title	Mean duration of worsening asthma symptoms associated with the presence of moderate or severe URTS or a confirmed RV infection

End point description:

A worsening asthma day is one on which any of the following occurred: rescue albuterol use above baseline, use of oral/parenteral corticosteroids for asthma, use of asthma medication other than study medication, asthma symptom scores >=3, nighttime awakenings, unscheduled health care visits, or missed school due to asthma. The duration of worsening asthma is the number of consecutive worsening asthma days after the date of a URTS score of 2 (moderate) or 3 (severe) or collection of a mucus sample containing RV (whichever occurred first). Each span of consecutive days is a participant interval.

ITT Population. Only those participants with relevant data defining a worsening asthma day during the peak viral period and with moderate or severe URTS or a confirmed RV infection were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121[6]	145[7]		
Units: Days per participant interval				
arithmetic mean (standard error)	4.1 (± 0.18)	4 (± 0.17)		

Notes:

[6] - ITT Population

[7] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of asthma exacerbations associated with the presence of moderate or severe URTS or a confirmed RV infection during the Peak Viral Period

End point title	Number of asthma exacerbations associated with the presence of moderate or severe URTS or a confirmed RV infection during the Peak Viral Period

End point description:

Each participant (with assistance from the parent/legal guardian as needed) was instructed to keep an electronic diary (eDiary) with record of daily URTS symptoms that included: runny nose, sneezing, nasal congestion, and sore throat. Based on the best-described aggregate URTS during the previous 24 hours, participants rated symptoms as: 0 = Not present; 1 = Mild, clearly present; 2 = Moderately severe, uncomfortable; and 3 = Severe, interfering with sleep or activity. Mucus samples were collected and analyzed for RV when the eDiary alerted for moderate/severe URTS.

ITT Population. Only those participants who reported >=1 exacerbation were analyzed. Only those participants with moderate or severe URTS or a confirmed RV infection were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[8]	7[9]		
Units: Number of asthma exacerbations	5	7		

Notes:

[8] - ITT Population

[9] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percentage of asthma-control days

End point title	Mean percentage of asthma-control days

End point description:

An asthma-control day was defined as a day without any of the following: rescue albuterol use, use of oral/parenteral corticosteroids for asthma, use of asthma medication other than double-blind study treatment, asthma symptom score >0, nighttime awakenings due to asthma, unscheduled health care visits (defined as home visits, office visits, or urgent care visits), ER visits, hospitalizations for asthma, or school absenteeism due to asthma. The percentage of asthma-control days = the number (No.) of asthma-control days divided by the No. of days of treatment exposure, multiplied by 100.

ITT Population. Only those participants who recorded data during the Peak Viral Period, had a treatment stop date with a defined Peak Viral Period, and had available data on all days on which data were recorded were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161[10]	156[11]		
Units: Percentage of days				
arithmetic mean (standard error)	48.3 (± 1.51)	49.7 (± 1.54)		

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percentage of episode-free (EF) days

End point title	Mean percentage of episode-free (EF) days

End point description:

An EF day was defined as a day without any of the following: rescue albuterol use, use of oral/parenteral corticosteroids for asthma, use of asthma medication other than study treatment, asthma symptom score >0, nighttime awakenings due to asthma, unscheduled health care visits (defined as home visits, office visits, or urgent care visits), ER visits, hospitalizations for asthma, school absenteeism due to asthma, or morning peak expiratory flow (measure of maximum airflow) <80% of baseline. Percentage of EF days=No. of EF days divided by No. of days of treatment exposure, multiplied by 100.

ITT Population. Only those participants who recorded data during the Peak Viral Period, had a treatment stop date with a defined Peak Viral Period, and had available data on all days on which data were recorded were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161[12]	155[13]		
Units: Percentage of days				
arithmetic mean (standard error)	42.4 (± 1.55)	44.5 (± 1.61)		

Notes:

[12] - ITT Population

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percentage of symptom-free days

End point title	Mean percentage of symptom-free days

End point description:

A symptom-free day was defined as a day during the Peak Viral Period on which the asthma symptom score was zero. The daily asthma symptom score (measured during the day and the previous night) was reported on a 6-point scale (ranging from 0=no symptoms to 5=severe symptoms). Percentage of symptom-free days was defined as the number of days during the Peak Viral Period on which the asthma symptom score=0, divided by the number of days in that same period on which non-missing values were recorded, multiplied by 100.

ITT Population. Only those participants who recorded data during the Peak Viral Period and had a treatment stop date with a defined Peak Viral Period were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161[14]	157[15]		
Units: Percentage of days				
arithmetic mean (standard deviation)	90.1 (± 15.89)	91.1 (± 13.18)		

Notes:

[14] - ITT Population

[15] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percentage of rescue-free days

End point title	Mean percentage of rescue-free days

End point description:

A rescue-free day was defined as a day during the Peak Viral Period on which no puffs of rescue medication were recorded. Percentage of rescue-free days was defined as the number of days during the Peak Viral Period on which no puffs of rescue medication were recorded, divided by the number of days in that same period on which non-missing values were recorded, multiplied by 100.

ITT Population. Only those participants who recorded data during the Peak Viral Period and had a treatment stop date with a defined Peak Viral Period were analyzed.

End point type	Secondary

End point timeframe:

Peak Viral Period (from 30 August 2010 through the end of treatment [up to Week 16])

End point values	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161[16]	157[17]		
Units: Percentage of days				
arithmetic mean (standard deviation)	92.1 (± 16.6)	91.7 (± 14.68)		

Notes:

[16] - ITT Population

[17] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants attended a total of 6 clinic visits (Baseline/Randomization, Weeks 1, 4, 8, 12, and 16) and received one follow-up phone call 7 days after the last clinic visit to assess for adverse events (AEs).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	FSC DISKUS 100/50 mcg BID

Reporting group description:

FSC at a dose of 100/50 mcg administered as one inhalation BID for 16 weeks

Reporting group title	FP DISKUS 100 mcg BID

Reporting group description:

FP DISKUS 100 mcg administered as one inhalation BID for 16 weeks

Serious adverse events	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 171 (1.17%)	1 / 168 (0.60%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 171 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	1 / 171 (0.58%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			
subjects affected / exposed	1 / 171 (0.58%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	1 / 171 (0.58%)	0 / 168 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytialviral			
subjects affected / exposed	1 / 171 (0.58%)	0 / 168 (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: 5 %

Non-serious adverse events	FSC DISKUS 100/50 mcg BID	FP DISKUS 100 mcg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 171 (54.39%)	94 / 168 (55.95%)	
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 171 (14.62%)	28 / 168 (16.67%)	
occurrences (all)	36	50	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	20 / 171 (11.70%)	16 / 168 (9.52%)	
occurrences (all)	25	22	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	9 / 171 (5.26%)	6 / 168 (3.57%)	
occurrences (all)	10	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	26 / 171 (15.20%)	21 / 168 (12.50%)	
occurrences (all)	35	25	
Nasal congestion			
subjects affected / exposed	15 / 171 (8.77%)	13 / 168 (7.74%)	
occurrences (all)	17	15	
Oropharyngeal pain			

subjects affected / exposed	14 / 171 (8.19%)	12 / 168 (7.14%)	
occurrences (all)	15	15	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	29 / 171 (16.96%)	31 / 168 (18.45%)	
occurrences (all)	35	41	
Nasopharyngitis			
subjects affected / exposed	15 / 171 (8.77%)	20 / 168 (11.90%)	
occurrences (all)	18	29	
Sinusitis			
subjects affected / exposed	11 / 171 (6.43%)	3 / 168 (1.79%)	
occurrences (all)	12	3	
Viral upper respiratory tract infection			
subjects affected / exposed	7 / 171 (4.09%)	9 / 168 (5.36%)	
occurrences (all)	8	17	
Otitis media			
subjects affected / exposed	3 / 171 (1.75%)	9 / 168 (5.36%)	
occurrences (all)	5	11	

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