Clinical trial results:
FFA112059: A randomised, double-blind, double-dummy, placebo controlled (with rescue medication), multicenter study to evaluate the efficacy and safety of fluticasone furoate inhalation powder in the treatment of persistent asthma in adults and adolescents.

Summary

EudraCT number	2010-020144-34
Trial protocol	BE DE Outside EU/EEA
Global end of trial date	16 January 2012

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	07 February 2015

Trial information

Trial identification

Sponsor protocol code	FFA112059

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 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of fluticasone furoate 100mcg administered once daily in the evening in adolescent and adult subjects 12 years of age and older with persistent bronchial asthma over a 24 week treatment period.

Protection of trial subjects:

The following withdrawal criteria for lack of efficacy were included:
A participant who met any of the following efficacy criteria was to have been withdrawn from the study:
1. Clinic FEV1 below the FEV1 stability limit value calculated at Visit 2
2. During the 7 days immediately preceding any visit, the participant experienced:
a) At least 4 days in which the PEF fell below the PEF Stability Limit calculated at Visit 2; OR
b) At least 3 days in which >=12 inhalations/day of albuterol/salbutamol were used.
3. Participants who experience a protocol-defined severe exacerbation, defined as deterioration of asthma requiring the use of systemic corticosteroids (tablets, suspension, or injection) for at least 3 days or an in-patient hospitalization or emergency department visit due to asthma that required systemic corticosteroids.
4. Clinical asthma worsening that in the opinion of the investigator requires additional asthma treatment other than study medication or study-supplied albuterol/salbutamol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 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	Poland: 94
Country: Number of subjects enrolled	Romania: 74
Country: Number of subjects enrolled	Belgium: 106
Country: Number of subjects enrolled	Germany: 67
Country: Number of subjects enrolled	United States: 695
Worldwide total number of subjects	1036
EEA total number of subjects	341

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)	121
Adults (18-64 years)	857
From 65 to 84 years	58
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One participant received treatment (placebo) but was not randomized. Thus, 350 participants were enrolled in the study; however, only 349 were randomized.

Pre-assignment

Screening details:

Participants (par.) meeting all inclusion criteria/no exclusion criteria during Visit 1 entered a 4-week Run-in Period (RIP). At Visit 2 (end of RIP), par. meeting the eligibility criteria were randomized to the 24-week Double blind Treatment Period. 1036 par. were screened, 349 were randomized, and 343 received >=1 dose of study treatment.

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 via a dry powder inhaler (DPI) once daily (OD) in the evening and placebo via the DISKUS/ACCUHALER twice daily (BID) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

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:

Matching placebo

Arm title	FF 100 µg OD

Arm description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a DPI OD in the evening plus placebo via the DISKUS/ACCUHALER BID for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

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 micrograms (µg) once daily

Arm title	FP 250 µg BID

Arm description:

Participants received fluticasone propionate (FP) 250 µg BID via the DISKUS/ACCUHALER plus placebo via a DPI OD in the evening (total daily dose of 500 µg) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

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:

250 µg twice daily

Number of subjects in period 1[1]	Placebo	FF 100 µg OD	FP 250 µg BID
Started	115	114	114
Completed	75	92	88
Not completed	40	22	26
Consent withdrawn by subject	10	3	3
Physician decision	-	-	3
Adverse event, non-fatal	2	2	3
Lost to follow-up	4	-	-
Lack of efficacy	23	15	14
Protocol deviation	1	2	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: Subject disposition data are collected for members of the Intent-to-Treat Population, defined as all randomized participants who received at least a single dose of trial medication. Not all participants enrolled in the trial (participants screened and for whom a record exists on the study database) were randomized to treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants received placebo via a dry powder inhaler (DPI) once daily (OD) in the evening and placebo via the DISKUS/ACCUHALER twice daily (BID) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FF 100 µg OD

Reporting group description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a DPI OD in the evening plus placebo via the DISKUS/ACCUHALER BID for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FP 250 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 250 µg BID via the DISKUS/ACCUHALER plus placebo via a DPI OD in the evening (total daily dose of 500 µg) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group values	Placebo	FF 100 µg OD	FP 250 µg BID
Number of subjects	115	114	114
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	40.3	40.1	41.4
standard deviation	± 17.68	± 16.17	± 15.64
Gender categorical Units: Subjects			
Female	68	63	72
Male	47	51	42
Race, customized Units: Subjects			
African American/African Heritage (HER)	23	22	19
Central/South Asian Heritage	1	0	1
Japanese/East Asian HER/South East Asian HER	1	1	1
Native Hawaiian or other Pacific Islander	1	0	0
White	88	90	92
American Indian or Alaska Native & White	1	0	0
Missing	0	1	1

Reporting group values	Total		
Number of subjects	343		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	203		
Male	140		
Race, customized Units: Subjects			
African American/African Heritage (HER)	64		
Central/South Asian Heritage	2		
Japanese/East Asian HER/South East Asian HER	3		
Native Hawaiian or other Pacific Islander	1		
White	270		
American Indian or Alaska Native & White	1		
Missing	2		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo via a dry powder inhaler (DPI) once daily (OD) in the evening and placebo via the DISKUS/ACCUHALER twice daily (BID) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FF 100 µg OD

Reporting group description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a DPI OD in the evening plus placebo via the DISKUS/ACCUHALER BID for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FP 250 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 250 µg BID via the DISKUS/ACCUHALER plus placebo via a DPI OD in the evening (total daily dose of 500 µg) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Primary: Mean change from Baseline in clinic visit trough evening (pre-bronchodilator and pre-dose) forced expiratory volume in one second (FEV1) at the end of the 24 week treatment period

End point title	Mean change from Baseline in clinic visit trough evening (pre-bronchodilator and pre-dose) forced expiratory volume in one second (FEV1) at the end of the 24 week treatment period

End point description:

FEV1 is a measure of lung function and is defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 is defined as the clinic visit (pre-bronchodilator and pre-dose) FEV1 measurement taken at the clinic visit at the end of the dosing interval. Pre-dose and pre-rescue albuterol/salbutamol trough FEV1 was measured electronically by spirometry in the evening at the Baseline through Week 24 clinic visits. The highest of 3 technically acceptable measurements was recorded. Baseline was the pre-dose value obtained at Visit 2. Change from Baseline was calculated as the Week 24 value minus the Baseline value. Analysis was performed using analysis of covariance (ANCOVA) with covariates of Baseline, region, 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.

End point type	Primary

End point timeframe:

Baseline and Week 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113[1]	111[2]	107[3]	
Units: Liters				
least squares mean (standard error)	0.015 (± 0.0394)	0.161 (± 0.0398)	0.159 (± 0.0406)	

Notes:

[1] - ITT Population. Only par. with non-missing covariates/post-Baseline FEV1 measurement were analyzed.
[2] - ITT Population. Only par. with non-missing covariates/post-Baseline FEV1 measurement were analyzed.
[3] - ITT Population. Only par. with non-missing covariates/post-Baseline FEV1 measurement were analyzed.

Statistical analyses

Statistical analysis title	Statistical Analysis #1
Comparison groups	Placebo v FF 100 µg OD
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	0.146
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.036
upper limit	0.257

Statistical analysis title	Statistical Analysis #2
Comparison groups	Placebo v FP 250 µg BID
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	0.145
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.033
upper limit	0.257

Secondary: Change from Baseline in the percentage of rescue-free 24-hour (hr) periods at the end of the 24-week Treatment Period

End point title	Change from Baseline in the percentage of rescue-free 24-hour (hr) periods at the end of the 24-week Treatment Period

End point description:

The number of inhalations of rescue bronchodilator, albuterol/salbutamol inhalation aerosol, used during the day and night was recorded by the participants in a daily electronic diary (eDiary). Similarly, 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 peak expiratory flow measurement. 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 to be rescue free. The Baseline value was derived from the last 7 days of the daily eDiary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 24-week Treatment Period 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 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114[4]	112[5]	113[6]	
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	6.5 (± 2.82)	21.3 (± 2.85)	24.3 (± 2.83)	

Notes:

[4] - ITT Population. Only those participants available at the specified time points were analyzed.

[5] - ITT Population. Only those participants available at the specified time points were analyzed.

[6] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in daily trough evening (PM) Peak Expiratory Flow (PEF) averaged over the first 12 weeks and 24 weeks of the 24-week Treatment Period

End point title	Mean change from Baseline in daily trough evening (PM) Peak Expiratory Flow (PEF) averaged over the first 12 weeks and 24 weeks of the 24-week Treatment Period

End point description:

PEF is a measure of lung function and 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 and evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. Trough evening PEF is the PM PEF measured approximately 24 hours after the last evening administration of study drug. Change from Baseline (defined as the last 7 days prior to randomization of the participants) was calculated as the value of the averaged daily trough PM PEF over 12 weeks and 24 weeks of the 24-week Treatment Period (at Weeks 12 and 24) 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:

From Baseline up to Week 12 and Week 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114[7]	112[8]	112[9]	
Units: Liters/minute (L/min)				
least squares mean (standard error)				
PM PEF, Week 1 to 12	0.4 (± 3.25)	2.2 (± 3.28)	4.8 (± 3.28)	
PM PEF, Week 1 to 24	-1.3 (± 3.36)	1.5 (± 3.39)	4.3 (± 3.4)	

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in daily morning (AM) PEF averaged over the first 12 weeks and 24 weeks of the 24-week Treatment Period

End point title	Mean change from Baseline in daily morning (AM) PEF averaged over the first 12 weeks and 24 weeks of the 24-week Treatment Period

End point description:

PEF is a measure of lung function and 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 and evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. Change from Baseline (defined as the last 7 days prior to randomization of the participants) was calculated as the value of the averaged daily AM PEF over 12 weeks and 24 weeks of the 24-week Treatment Period (at Weeks 12 and 24) 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:

From Baseline up to Week 12 and Week 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114[10]	112[11]	113[12]	
Units: Liters/minute (L/min)				
least squares mean (standard error)				
AM PEF, Week 1 to 12	5.7 (± 3.41)	13.2 (± 3.44)	9.4 (± 3.43)	
AM PEF, Week 1 to 24	5 (± 3.45)	13.9 (± 3.48)	9.9 (± 3.47)	

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the percentage of symptom-free 24-hour (hr) periods at the end of the 24-week Treatment Period

End point title	Change from Baseline in the percentage of symptom-free 24-hour (hr) periods at the end of the 24-week Treatment Period

End point description:

The number of inhalations of rescue bronchodilator, albuterol/salbutamol inhalation aerosol, used during the day and night was recorded by the participants in a daily electronic diary (eDiary). Similarly, 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 peak expiratory flow measurement. A 24-hour 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 value was derived from the last 7 days of the daily eDiary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 24-week Treatment Period 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 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114[13]	112[14]	113[15]	
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	10.4 (± 2.77)	19.3 (± 2.79)	19.2 (± 2.78)	

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the total Asthma Quality of Life Questionnaire (AQLQ) (+12) score at Week 12 and Week 24

End point title	Change from Baseline in the total Asthma Quality of Life Questionnaire (AQLQ) (+12) score at Week 12 and Week 24

End point description:

The AQLQ is a disease-specific, self-administered quality of life questionnaire used to evaluate the impact of asthma treatments on the quality of life of asthma sufferers. The AQLQ for 12 years and older (AQLQ [+12]) is a modified version of the AQLQ for use in asthma patients between the ages of 12 and 70. The AQLQ contains 32 items in 4 domains: activity limitation (11 items), symptoms (12 items), emotional function (5 items), and environmental stimuli (4 items). For the 32 items on the questionnaire, the response format consists of a seven-point scale, where a value of 1 indicates "total impairment" and a value of 7 indicates "no impairment." The AQLQ total score is defined as the average of the scores from all 32 questions; thus, the total score ranges from 1 (indicates "total impairment") to 7 (indicates "no impairment"). Baseline was the total score obtained at Visit 3. Change from Baseline was calculated as the total score at Weeks 12 and 24 minus the total score at Baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 12, and Week 24

End point values	Placebo	FF 100 µg OD	FP 250 µg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[16]	114[17]	114[18]	
Units: Scores on a scale				
least squares mean (standard error)				
Week 12, n=85, 99, 99	0.45 (± 0.078)	0.69 (± 0.072)	0.73 (± 0.073)	

Week 24, n=74, 90, 86	0.51 (± 0.09)	0.84 (± 0.082)	0.67 (± 0.084)	

Notes:

[16] - ITT Population. Par. available at the specified time points were analyzed (n=X, X, X in categories).

[17] - ITT Population. Par. available at the specified time points were analyzed (n=X, X, X in categories).

[18] - ITT Population. Par. available at the specified time points were analyzed (n=X, X, X in categories).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication to the end of the treatment period (up to Week 24).

Adverse event reporting additional description:

An on-therapy AE or SAE is defined as an AE with an onset on or after the start date of study medication, but not later than one day after the last date of study medication. SAEs and AEs were collected in members of the ITT Population, comprised of all participants randomized to treatment, who received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo via a dry powder inhaler (DPI) once daily (OD) in the evening and placebo via the DISKUS/ACCUHALER twice daily (BID) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FF 100 µg OD

Reporting group description:

Participants received fluticasone furoate (FF) 100 microgram (µg) inhalation powder via a DPI OD in the evening plus placebo via the DISKUS/ACCUHALER BID for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Reporting group title	FP 250 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 250 µg BID via the DISKUS/ACCUHALER plus placebo via a DPI OD in the evening (total daily dose of 500 µg) for 24 weeks (168 days). In addition, all participants were provided with albuterol/salbutamol aerosol to be used as rescue medication as needed.

Serious adverse events	Placebo	FF 100 µg OD	FP 250 µg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 115 (1.74%)	4 / 114 (3.51%)	1 / 114 (0.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 115 (0.00%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			

subjects affected / exposed	0 / 115 (0.00%)	0 / 114 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn’s disease			
subjects affected / exposed	0 / 115 (0.00%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Epididymal cyst			
subjects affected / exposed	0 / 115 (0.00%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 115 (0.00%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 114 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	FF 100 µg OD	FP 250 µg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 115 (26.09%)	37 / 114 (32.46%)	19 / 114 (16.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 115 (4.35%)	7 / 114 (6.14%)	7 / 114 (6.14%)
occurrences (all)	6	7	12
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 115 (3.48%)	1 / 114 (0.88%)	0 / 114 (0.00%)
occurrences (all)	4	1	0
Sinusitis			
subjects affected / exposed	1 / 115 (0.87%)	4 / 114 (3.51%)	2 / 114 (1.75%)
occurrences (all)	1	4	2
Pharyngitis			
subjects affected / exposed	4 / 115 (3.48%)	5 / 114 (4.39%)	2 / 114 (1.75%)
occurrences (all)	4	5	2
Bronchitis			
subjects affected / exposed	7 / 115 (6.09%)	8 / 114 (7.02%)	4 / 114 (3.51%)
occurrences (all)	7	9	4
Nasopharyngitis			
subjects affected / exposed	6 / 115 (5.22%)	9 / 114 (7.89%)	4 / 114 (3.51%)
occurrences (all)	6	11	6
Upper respiratory tract infection			
subjects affected / exposed	6 / 115 (5.22%)	7 / 114 (6.14%)	6 / 114 (5.26%)
occurrences (all)	7	7	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 January 2011	Amendment of entry criteria to make study population more representative of the population that will ultimately use the product once marketed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported