Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter, Two-Year Study to Evaluate the Ocular Safety of Once-Daily, Fluticasone Furoate Nasal Spray 110mcg in Adults and Adolescents 12 Years of Age and Older with Perennial Allergic Rhinitis

Summary

EudraCT number	2015-004891-31
Trial protocol	Outside EU/EEA
Global end of trial date	18 February 2011

Results information

Result version number	v1 (current)
This version publication date	22 January 2017
First version publication date	22 January 2017

Trial information

Trial identification

Sponsor protocol code	FFR110537

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	29 March 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2011
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	30 June 2008
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: 548
Worldwide total number of subjects	548
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)	66
Adults (18-64 years)	475
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total 548 participants were randomized into the study.

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:

The matching placebo nasal spray containing only fluticasone furoate (FF) vehicle was self-administered as two sprays per nostril each morning once daily (QD) for 104 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Self-administration of Placebo two sprays per nostril each morning once daily

Arm title	FF 110 mcg QD

Arm description:

FF nasal spray aqueous suspension contained 0.05% micronized FF. Each spray contained approximately 27.5 micrograms (mcg) of FF; participants self-administered two sprays per nostril each morning QD for a total dose of 110 mcg for 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Furoate (FF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

Self-administration of FF nasal spray: two sprays per nostril each morning QD for a total dose of 110 mcg

Number of subjects in period 1	Placebo	FF 110 mcg QD
Started	181	367
Completed	104	199
Not completed	77	168
Physician decision	2	6
Consent withdrawn by subject	19	53
Met Protocol-defined Stopping Criteria	3	4
Adverse event, non-fatal	12	23
Lost to follow-up	1	6
Lack of efficacy	2	-
Protocol deviation	38	76

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
The matching placebo nasal spray containing only fluticasone furoate (FF) vehicle was self-administered as two sprays per nostril each morning once daily (QD) for 104 weeks.	
Reporting group title	FF 110 mcg QD
Reporting group description:	
FF nasal spray aqueous suspension contained 0.05% micronized FF. Each spray contained approximately 27.5 micrograms (mcg) of FF; participants self-administered two sprays per nostril each morning QD for a total dose of 110 mcg for 104 weeks.	

Reporting group values	Placebo	FF 110 mcg QD	Total
Number of subjects	181	367	548
Age categorical			
Units: Subjects			
Age continuous			
Baseline Characteristics were collected in members of the Intent-to-Treat (ITT) Population, comprised of all participants who were randomized and received at least one dose of double-blind study drug. One participant in the placebo group and one participant in the FF 110 mcg QD group did not receive any study drug and were thus not included in the ITT Population.			
Units: years			
arithmetic mean	38	37	
standard deviation	± 13.34	± 13.48	-
Gender categorical			
Baseline Characteristics were collected in members of the Intent-to-Treat (ITT) Population, comprised of all participants who were randomized and received at least one dose of double-blind study drug. One participant in the placebo group and one participant in the FF 110 mcg QD group did not receive any study drug and were thus not included in the ITT Population.			
Units: Subjects			
Female	116	255	371
Male	65	112	177
Race/Ethnicity, Customized			
Baseline Characteristics were collected in members of the Intent-to-Treat (ITT) Population, comprised of all participants who were randomized and received at least one dose of double-blind study drug. One participant in the placebo group and one participant in the FF 110 mcg QD group did not receive any study drug and were thus not included in the ITT Population.			
Units: Subjects			
African American/African Heritage	29	50	79
American Indian or Alaska Native	1	4	5
Central/South Asian Heritage	0	1	1
Japanese/East Asian/South East Asian Heritage	2	6	8
Mixed Asian Heritage	0	1	1
Native Hawaiian or other Pacific Islander	2	2	4
White	146	303	449
African American/African Heritage & White	1	0	1

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

The matching placebo nasal spray containing only fluticasone furoate (FF) vehicle was self-administered as two sprays per nostril each morning once daily (QD) for 104 weeks.

Reporting group title	FF 110 mcg QD

Reporting group description:

FF nasal spray aqueous suspension contained 0.05% micronized FF. Each spray contained approximately 27.5 micrograms (mcg) of FF; participants self-administered two sprays per nostril each morning QD for a total dose of 110 mcg for 104 weeks.

Primary: Cumulative proportion (CU) of participants (par.) with an event, as measured as a percentage, for posterior subcapsular opacity (P)

End point title	Cumulative proportion (CU) of participants (par.) with an event, as measured as a percentage, for posterior subcapsular opacity (P)

End point description:

An event for P (opacity in the lens positioned just anterior to the posterior lens capsule and characterized by the posterior migration of lens epithelial cells from the lens bow) is defined as an increase of >=0.3 from baseline in Lens Opacities Classification System, Version III (LOCS III; system used for the grading and comparison of cataract severity and type based on standard color photographic transparencies) grade for P (range=0.1 [lens clear] to 5.9 [lens unclear]), in either eye. Data represent the Kaplan-Meier estimate for the CU of par. with an event of P based on a lifetest table. ITT Population: All participants (par.) with post-base line ophthalmic examination data were included in the analysis for this endpoint. Par. without post-base line ophthalmic exam data were censored at the randomization data . Par. who completed the study without an event for P or were discontinued for reasons other than an event for P were censored.

End point type	Primary

End point timeframe:

Baseline; Weeks 12, 24, 36, 52, 64, 76, 88, and 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168[1]	344		
Units: Percentage of participants				
number (not applicable)				
Week 12	0.6	0.88		
Week 24	1.24	1.84		
Week 36	1.93	2.56		
Week 52	2.68	3.72		
Week 64	2.68	3.72		
Week 76	2.68	3.72		
Week 88	2.68	4.59		
Week 104	2.68	5.09		

Notes:

[1] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	FF 110 mcg QD v Placebo
Number of subjects included in analysis	512
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.395
Method	Wald Chi-square

Notes:

[2] - Wald Chi-Square test based on a proportional hazards model adjusting for age and baseline value

Primary: Cumulative proportion of participants, as measured as a percentage, with an intraocular pressure (IOP) event

End point title	Cumulative proportion of participants, as measured as a percentage, with an intraocular pressure (IOP) event

End point description:

An event for IOP is defined as an increase of 7 millimeters of mercury (mm Hg) or greater from baseline in IOP, in either eye, using Goldmann Applanation Tonometry (GAT). GAT is a commonly used method of determining approximate intraocular pressure. The data below represent the Kaplan-Meier estimate for the cumulative proportion of participants with an IOP event based on a lifetest table.

End point type	Primary

End point timeframe:

Baseline; Weeks 12, 24, 36, 52, 64, 76, 88, and 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168[3]	344		
Units: percentage of participants				
number (not applicable)				
Week 12	0	0		
Week 24	0	0.32		
Week 36	0	0.32		
Week 52	0	0.71		
Week 64	0	1.12		
Week 76	0	1.98		
Week 88	0.84	1.98		
Week 104	0.84	2.96		

Notes:

[3] - ITT population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 mcg QD

Number of subjects included in analysis	512
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.342
Method	Wald Chi-square

Notes:

[4] - Wald Chi-Square test based on a proportional hazards model adjusting for age and baseline value

Secondary: Change from baseline in LOCS III Posterior Subcapsular Opacity at Week 52 and Week 104

End point title	Change from baseline in LOCS III Posterior Subcapsular Opacity at Week 52 and Week 104

End point description:

An event for P (opacity in the lens positioned just anterior to the posterior lens capsule and characterized by the posterior migration of lens epithelial cells from the lens bow) is defined as an increase of >=0.3 from baseline in LOCS III (system used for the grading and comparison of cataract severity and type based on standard color photographic transparencies) grade for P (range=0.1 [lens clear] to 5.9 [lens unclear]), in either eye. Change from baseline was calculated by subtracting the baseline value from the Week 52 and Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[5]	198		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	0 (± 0.042)	0 (± 0.063)		
Left eye, Week 104; n=104, 198	0 (± 0.039)	0 (± 0.083)		
Right eye, Week 52; n=130, 251	0 (± 0.057)	0 (± 0.061)		
Right eye, Week 104; n=104, 198	0 (± 0.042)	-0.01 (± 0.068)		

Notes:

[5] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated change from baseline in LOCS III posterior subcapsular opacity by increments of 0.1 at Weeks 52 and 104

End point title	Number of participants with the indicated change from baseline in LOCS III posterior subcapsular opacity by increments of 0.1 at Weeks 52 and 104

End point description:

An event for P is defined as an increase of >=0.3 from baseline in LOCS III (classification system based on standard color photographic transparencies) grade for P (range=0.1 [lens clear] to 5.9 [lens unclear]), in either eye. Change from baseline was calculated by subtracting the baseline value from the Week 52 and Week 104 value.

End point type	Secondary

End point timeframe:
Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[6]	251		
Units: participants				
Left eye, Week 52, <-0.3; n=130, 251	0	0		
Left eye, Week 52, -0.3; n=130, 251	0	0		
Left eye, Week 52, -0.2; n=130, 251	2	5		
Left eye, Week 52, -0.1; n=130, 251	3	13		
Left eye, Week 52, 0; n=130, 251	121	218		
Left eye, Week 52, 0.1; n=130, 251	3	12		
Left eye, Week 52, 0.2; n=130, 251	0	0		
Left eye, Week 52, 0.3; n=130, 251	1	2		
Left eye, Week 52, 0.4; n=130, 251	0	0		
Left eye, Week 52, 0.5; n=130, 251	0	0		
Left eye, Week 52, 0.6; n=130, 251	0	1		
Left eye, Week 52, 0.7; n=130, 251	0	0		
Left eye, Week 52, 0.8; n=130, 251	0	0		
Left eye, Week 52, >=0.9; n=130, 251	0	0		
Left eye, Week 52, >=0.3; n=130, 251	1	3		
Left eye, Week 52, >=0.5; n=130, 251	0	1		
Left eye, Week 52, >=1.0; n=130, 251	0	0		
Right eye, Week 52, <-0.3; n=130, 251	0	0		
Right eye, Week 52, -0.3; n=130, 251	1	0		
Right eye, Week 52, -0.2; n=130, 251	1	5		
Right eye, Week 52, -0.1; n=130, 251	0	10		
Right eye, Week 52, 0; n=130, 251	122	218		
Right eye, Week 52, 0.1; n=130, 251	4	13		
Right eye, Week 52, 0.2; n=130, 251	0	2		
Right eye, Week 52, 0.3; n=130, 251	1	1		
Right eye, Week 52, 0.4; n=130, 251	1	2		
Right eye, Week 52, 0.5; n=130, 251	0	0		
Right eye, Week 52, 0.6; n=130, 251	0	0		
Right eye, Week 52, 0.7; n=130, 251	0	0		
Right eye, Week 52, 0.8; n=130, 251	0	0		
Right eye, Week 52, >=0.9; n=130, 251	0	0		
Right eye, Week 52, >=0.3; n=130, 251	2	3		
Right eye, Week 52, >=0.5; n=130, 251	0	0		
Right eye, Week 52, >=1.0; n=130, 251	0	0		
Left eye, Week 104, <-0.3; n=104, 198	0	0		
Left eye, Week 104, -0.3; n=104, 198	0	0		
Left eye, Week 104, -0.2; n=104, 198	2	5		
Left eye, Week 104, -0.1; n=104, 198	3	11		
Left eye, Week 104, 0; n=104, 198	94	175		

Left eye, Week 104, 0.1; n=104, 198	5	5		
Left eye, Week 104, 0.2; n=104, 198	0	0		
Left eye, Week 104, 0.3; n=104, 198	0	0		
Left eye, Week 104, 0.4; n=104, 198	0	0		
Left eye, Week 104, 0.5; n=104, 198	0	0		
Left eye, Week 104, 0.6; n=104, 198	0	1		
Left eye, Week 104, 0.7; n=104, 198	0	0		
Left eye, Week 104, 0.8; n=104, 198	0	1		
Left eye, Week 104, >=0.9; n=104, 198	0	0		
Left eye, Week 104, >=0.3; n=104, 198	0	2		
Left eye, Week 104, >=0.5; n=104, 198	0	2		
Left eye, Week 104, >=1.0; n=104, 198	0	0		
Right eye, Week 104, <-0.3; n=104, 198	0	0		
Right eye, Week 104, -0.3; n=104, 198	1	0		
Right eye, Week 104, -0.2; n=104, 198	1	5		
Right eye, Week 104, -0.1; n=104, 198	2	14		
Right eye, Week 104, 0; n=104, 198	97	174		
Right eye, Week 104, 0.1; n=104, 198	3	2		
Right eye, Week 104, 0.2; n=104, 198	0	2		
Right eye, Week 104, 0.3; n=104, 198	0	0		
Right eye, Week 104, 0.4; n=104, 198	0	0		
Right eye, Week 104, 0.5; n=104, 198	0	0		
Right eye, Week 104, 0.6; n=104, 198	0	0		
Right eye, Week 104, 0.7; n=104, 198	0	1		
Right eye, Week 104, 0.8; n=104, 198	0	0		
Right eye, Week 104, >=0.9; n=104, 198	0	0		
Right eye, Week 104, >=0.3; n=104, 198	0	1		
Right eye, Week 104, >=0.5; n=104, 198	0	1		
Right eye, Week 104, >=1.0; n=104, 198	0	0		

Notes:

[6] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in LOCS III cortical opacity (C) at Week 52 and Week 104

End point title	Change from baseline in LOCS III cortical opacity (C) at Week 52 and Week 104

End point description:

An event for C (an opacity starting at the outer edge of the lens and progressing toward the center) is defined as an increase of >=0.3 from baseline in LOCS III (system used for the grading and comparison of cataract severity and type based on standard color photographic transparencies) grade for C (range=0.1 [lens clear] to 5.9 [lens unclear]), in either eye. Change from baseline was calculated by subtracting the baseline value from the Week 52 and Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[7]	251		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	0.01 (± 0.21)	0 (± 0.113)		
Left eye, Week 104; n=104, 198	0.02 (± 0.21)	0.01 (± 0.186)		
Right eye, Week 52; n=130, 251	-0.01 (± 0.229)	0 (± 0.154)		
Right eye, Week 104; n=104, 198	0.02 (± 0.187)	0.01 (± 0.186)		

Notes:

[7] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated change from baseline in cortical opacity by increment categories of >=0.3, >=0.5, and >=1.0 at Weeks 52 and 104

End point title	Number of participants with the indicated change from baseline in cortical opacity by increment categories of >=0.3, >=0.5, and >=1.0 at Weeks 52 and 104

End point description:

An event for C (an opacity starting at the outer edge of the lens and progressing toward the center) is defined as an increase of >=0.3 from baseline in LOCS III (system used for the grading and comparison of cataract severity and type based on standard color photographic transparencies) grade for C (range=0.1 [lens clear] to 5.9 [lens unclear]), in either eye. Change from baseline was calculated by subtracting the baseline value from the Week 52 and Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[8]	251		
Units: participants				
Left eye, Week 52, >=0.3; n=130, 251	4	4		
Left eye, Week 52, >=0.5; n=130, 251	1	0		
Left eye, Week 52, >=1.0; n=130, 251	1	0		
Right eye, Week 52, >=0.3; n=130, 251	3	8		
Right eye, Week 52, >=0.5; n=130, 251	1	2		
Right eye, Week 52, >=1.0; n=130, 251	1	0		
Left eye, Week 104, >=0.3; n=104, 198	6	10		

Left eye, Week 104, >=0.5; n=104, 198	3	4		
Left eye, Week 104, >=1.0; n=104, 198	1	1		
Right eye, Week 104, >=0.3; n=104, 198	3	10		
Right eye, Week 104, >=0.5; n=104, 198	2	4		
Right eye, Week 104, >=1.0; n=104, 198	1	2		

Notes:

[8] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in LOCS III Nuclear Opacity (NO) at Week 52 and Week 104

End point title	Change from baseline in LOCS III Nuclear Opacity (NO) at Week 52 and Week 104

End point description:

Nuclear opacity refers to the opacity in the central nucleus of the eye.The range for NO is 0.1 (no opacity) to 6.9 (maximum opacity). Change from baseline in NO was calculated by subtracting the baseline value from the Week 52 or Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[9]	251		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	0.12 (± 0.498)	0.06 (± 0.495)		
Left eye, Week 104; n=104, 198	0.21 (± 0.538)	0.1 (± 0.506)		
Right eye, Week 52; n=130, 251	0.12 (± 0.511)	0.06 (± 0.492)		
Right eye, Week 104; n=104, 198	0.21 (± 0.55)	0.09 (± 0.531)		

Notes:

[9] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Nuclear Color (NC) at Week 52 and Week 104

End point title	Change from baseline in Nuclear Color (NC) at Week 52 and Week 104

End point description:

Nuclear color is associated with the force required to compress a lens to 75% of its original depth. The range for NC is 0.1 (no opacity) to 6.9 (maximum opacity). Change from baseline in NC was calculated by subtracting the baseline value from the Week 52 or Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[10]	251		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	0.14 (± 0.432)	0.09 (± 0.402)		
Left eye, Week 104; n=104, 198	0.21 (± 0.454)	0.13 (± 0.465)		
Right eye, Week 52; n=130, 251	0.16 (± 0.422)	0.09 (± 0.41)		
Right eye, Week 104; n=104, 198	0.22 (± 0.452)	0.13 (± 0.469)		

Notes:

[10] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in intraocular pressure (IOP) at Weeks 52 and 104

End point title	Change from baseline in intraocular pressure (IOP) at Weeks 52 and 104

End point description:

An event for IOP is defined as an increase of 7 mm Hg or greater from baseline in IOP, in either eye, using Goldmann Applanation Tonometry. Participants without post-baseline ophthalmic exam data were censored at the randomization date. Change from baseline was calculated by subtracting the baseline value from the Week 52 or Week 104 value.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[11]	251		
Units: mm Hg				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	-0.5 (± 2.04)	-0.3 (± 2.26)		
Left eye, Week 104; n=104, 198	-0.8 (± 1.98)	-0.6 (± 2.41)		
Right eye, Week 52; n=130, 251	-0.7 (± 2.08)	-0.4 (± 2.33)		
Right eye, Week 104; n=104, 198	-1 (± 2.17)	-0.7 (± 2.55)		

Notes:

[11] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated change from baseline in intraocular pressure (IOP) by increments of 1 mm Hg at Week 52

End point title	Number of participants with the indicated change from baseline in intraocular pressure (IOP) by increments of 1 mm Hg at Week 52

End point description:

An event for IOP is defined as an increase of 7 mm Hg or greater from baseline in IOP, in either eye, using Goldmann Applanation Tonometry. Participants without post-baseline ophthalmic exam data were censored at the randomization date. Change from baseline was calculated by subtracting the baseline value from the Week 52 value.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[12]	251		
Units: participants				
Left eye, IOP = <-10 to -9	1	0		
Left eye, IOP = -8	0	0		
Left eye, IOP = -7	0	2		
Left eye, IOP = -6	0	0		
Left eye, IOP = -5	3	3		
Left eye, IOP = -4	5	12		
Left eye, IOP = -3	9	19		
Left eye, IOP = -2	18	40		
Left eye, IOP = -1	22	40		
Left eye, IOP = 0	36	50		
Left eye, IOP = 1	20	30		
Left eye, IOP = 2	7	24		
Left eye, IOP = 3	5	19		
Left eye, IOP = 4	4	7		
Left eye, IOP = 5	0	3		
Left eye, IOP = 6	0	2		
Left eye, IOP = 7	0	0		
Left eye, IOP = 8	0	0		
Left eye, IOP = 9	0	0		
Left eye, IOP >= 7	0	0		
Left eye, IOP >= 10	0	0		
Left eye, IOP >= 15	0	0		
Right eye, IOP = <-10 to -9	0	0		
Right eye, IOP = -8	0	1		
Right eye, IOP = -7	2	0		
Right eye, IOP = -6	0	1		
Right eye, IOP = -5	2	4		
Right eye, IOP = -4	7	14		

Right eye, IOP = -3	9	23		
Right eye, IOP = -2	25	43		
Right eye, IOP = -1	22	34		
Right eye, IOP = 0	28	46		
Right eye, IOP = 1	16	31		
Right eye, IOP = 2	13	27		
Right eye, IOP = 3	3	14		
Right eye, IOP = 4	2	8		
Right eye, IOP = 5	1	2		
Right eye, IOP = 6	0	3		
Right eye, IOP = 7	0	0		
Right eye, IOP = 8	0	0		
Right eye, IOP = 9	0	0		
Right eye, IOP >= 7	0	0		
Right eye, IOP >= 10	0	0		
Right eye, IOP >= 15	0	0		

Notes:

[12] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated change from baseline in intraocular pressure (IOP) by increments of 1 mm Hg at Week 104

End point title	Number of participants with the indicated change from baseline in intraocular pressure (IOP) by increments of 1 mm Hg at Week 104

End point description:

An event for IOP is defined as an increase of 7 mm Hg or greater from baseline in IOP, in either eye, using Goldmann Applanation Tonometry. Participants without post-baseline ophthalmic exam data were censored at the randomization date. Change from baseline in IOP was calculated by subtracting the baseline value from the Week 104 value.

End point type	Secondary

End point timeframe:

Baseline and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104[13]	198		
Units: participants				
Left eye, IOP = <-10 to -9	0	0		
Left eye, IOP = -8	0	1		
Left eye, IOP = -7	0	0		
Left eye, IOP = -6	2	3		
Left eye, IOP = -5	0	7		
Left eye, IOP = -4	6	10		
Left eye, IOP = -3	15	19		
Left eye, IOP = -2	17	31		
Left eye, IOP = -1	15	32		

Left eye, IOP = 0	21	32		
Left eye, IOP = 1	19	30		
Left eye, IOP = 2	5	16		
Left eye, IOP = 3	3	7		
Left eye, IOP = 4	0	6		
Left eye, IOP = 5	1	2		
Left eye, IOP = 6	0	1		
Left eye, IOP = 7	0	1		
Left eye, IOP = 8	0	0		
Left eye, IOP = 9	0	0		
Left eye, IOP >= 7	0	1		
Left eye, IOP >= 10	0	0		
Left eye, IOP >= 15	0	0		
Right eye, IOP = <-10 to -9	0	0		
Right eye, IOP = -8	0	1		
Right eye, IOP = -7	0	2		
Right eye, IOP = -6	2	1		
Right eye, IOP = -5	5	7		
Right eye, IOP = -4	4	15		
Right eye, IOP = -3	10	17		
Right eye, IOP = -2	24	32		
Right eye, IOP = -1	21	22		
Right eye, IOP = 0	12	46		
Right eye, IOP = 1	16	23		
Right eye, IOP = 2	6	13		
Right eye, IOP = 3	1	8		
Right eye, IOP = 4	1	5		
Right eye, IOP = 5	1	2		
Right eye, IOP = 6	1	2		
Right eye, IOP = 7	0	2		
Right eye, IOP = 8	0	0		
Right eye, IOP = 9	0	0		
Right eye, IOP >= 7	0	2		
Right eye, IOP >= 10	0	0		
Right eye, IOP >= 15	0	0		

Notes:

[13] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in logarithm of the Minimum Angle of Resolution (LogMAR) visual acuity (VA) using Early Treatment Diabetic Retinopathy Study (ETDRS) charts at Week 52 and Week 104

End point title	Change from baseline in logarithm of the Minimum Angle of Resolution (LogMAR) visual acuity (VA) using Early Treatment Diabetic Retinopathy Study (ETDRS) charts at Week 52 and Week 104

End point description:

ETDRS charts are used to measure VA (the ability to resolve fine image details). Participants must have had a best-corrected distance VA of =< 0.18 on the LogMAR scale using ETDRS charts in both eyes measured separately. The LogMAR scale (expressed as the [decadic] logarithm of the minimum angle of

resolution [range from +1.00 to -0.30]) converts the geometric sequence of a traditional chart to a linear scale. It measures VA loss; positive values indicate vision loss, whereas negative values denote normal or better VA. A lower LogMAR value indicates better VA.

End point type	Secondary

End point timeframe:

Baseline, Week 52, and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[14]	251		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Left eye, Week 52; n=130, 251	-0.027 (± 0.0729)	-0.013 (± 0.0778)		
Left eye, Week 104; n=104, 198	-0.035 (± 0.074)	-0.023 (± 0.0858)		
Right eye, Week 52; n=130, 251	-0.023 (± 0.081)	-0.014 (± 0.0852)		
Right eye, Week 104; n=104, 198	-0.025 (± 0.0992)	-0.024 (± 0.0899)		

Notes:

[14] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in the funduscopic horizontal cup-to-disc ratio at Week 104

End point title	Percent change from baseline in the funduscopic horizontal cup-to-disc ratio at Week 104

End point description:

The funduscopic horizontal cup-to-risk ratio assesses the progression of glaucoma. Percent change from baseline in funduscopic horizontal cup-to-disc ratio at Week 104 was calculated by substracting the baseline value from the Week 104 value (both expressed as a percent). The cup-to-disc ratio compares the diameter of the "cup" portion of the optic disc with the total diameter of the optic disc. A large cup-to-disc ratio may imply glaucoma or other pathology.

End point type	Secondary

End point timeframe:

Baseline and Week 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104[15]	198		
Units: percent change				
arithmetic mean (standard deviation)				
Left eye	0 (± 7.23)	0.7 (± 7.58)		
Right eye	0 (± 7.31)	0 (± 7.39)		

Notes:

[15] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the daily reflective total nasal symptom score (rTNSS) for the indicated study periods

End point title	Change from baseline in the daily reflective total nasal symptom score (rTNSS) for the indicated study periods

End point description:

rTNSS was evaluated on a 4-point categorical scale (sum of the scores for rhinorrhea, nasal congestion, nasal itching, and sneezing; range=0-12). The data collected were used as a measure for treatment compliance. The scores on the scale were based on the severity of each nasal symptom: 0=none (symptom is not present); 1=mild (sign/symptom is clearly present but minimal awareness; easily tolerated); 2=moderate (definite awareness of sign/symptom that is bothersome but tolerable); 3=severe (sign/symptom is hard to tolerate; causes interference with activities of daily living and/or sleeping).

End point type	Secondary

End point timeframe:

Baseline, Weeks 1 to 26, Weeks 27 to 52, Weeks 53 to 78, and Weeks 79 to 104

End point values	Placebo	FF 110 mcg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181[16]	367		
Units: scores on a scale				
least squares mean (standard error)				
Week 1 to 26	-2.12 (± 0.17)	-3.19 (± 0.12)		
Week 27 to 52	-2.52 (± 0.21)	-3.86 (± 0.15)		
Week 53 to 78	-2.56 (± 0.23)	-3.89 (± 0.16)		
Week 79 to 104	-2.59 (± 0.25)	-4.1 (± 0.18)		
Week 1 to 104	-2.3 (± 0.18)	-3.45 (± 0.13)		

Notes:

[16] - ITT population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study drug to Visit 29 (7 days following Visit 28 or early withdrawal)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
The matching placebo nasal spray containing only fluticasone furoate (FF) vehicle was self-administered as two sprays per nostril each morning once daily (QD) for 104 weeks.	
Reporting group title	FF 110 mcg QD
Reporting group description:	
FF nasal spray aqueous suspension contained 0.05% micronized FF. Each spray contained approximately 27.5 micrograms (mcg) of FF; participants self-administered two sprays per nostril each morning QD for a total dose of 110 mcg for 104 weeks.	

Serious adverse events	Placebo	FF 110 mcg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 181 (3.87%)	12 / 367 (3.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 181 (0.00%)	2 / 367 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-uterine death			
subjects affected / exposed	1 / 181 (0.55%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
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			
Bronchospasm			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper airway obstruction			
subjects affected / exposed	1 / 181 (0.55%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 181 (0.55%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood pressure increased			

subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eye disorders			
Vitreous floaters			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 181 (1.10%)	0 / 367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 181 (0.00%)	1 / 367 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	FF 110 mcg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 181 (53.59%)	232 / 367 (63.22%)	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 181 (7.18%)	29 / 367 (7.90%)	
occurrences (all)	28	60	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	34 / 181 (18.78%)	123 / 367 (33.51%)	
occurrences (all)	58	254	
Oropharyngeal pain			
subjects affected / exposed	9 / 181 (4.97%)	23 / 367 (6.27%)	
occurrences (all)	13	27	
Nasal ulcer			
subjects affected / exposed	3 / 181 (1.66%)	30 / 367 (8.17%)	
occurrences (all)	3	36	
Nasal septum ulceration			
subjects affected / exposed	6 / 181 (3.31%)	24 / 367 (6.54%)	
occurrences (all)	7	34	
Infections and infestations			
Sinusitis			
subjects affected / exposed	31 / 181 (17.13%)	47 / 367 (12.81%)	
occurrences (all)	45	63	
Upper respiratory tract infection			
subjects affected / exposed	29 / 181 (16.02%)	52 / 367 (14.17%)	
occurrences (all)	58	89	
Nasopharyngitis			
subjects affected / exposed	17 / 181 (9.39%)	44 / 367 (11.99%)	
occurrences (all)	28	64	
Influenza			
subjects affected / exposed	16 / 181 (8.84%)	25 / 367 (6.81%)	
occurrences (all)	16	26	
Viral upper respiratory tract infection			
subjects affected / exposed	12 / 181 (6.63%)	27 / 367 (7.36%)	
occurrences (all)	19	36	
Bronchitis			

subjects affected / exposed	8 / 181 (4.42%)	31 / 367 (8.45%)	
occurrences (all)	10	43	
Acute sinusitis			
subjects affected / exposed	7 / 181 (3.87%)	20 / 367 (5.45%)	
occurrences (all)	7	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2008	This amendment added a medical monitor to contact sponsor information, Included additional Exclusion Criteria, Allowed re-screening of subjects, Clarified all subjects should have a post-treatment follow-up visit, Clarified when follow-up ophthalmic examinations are required for subjects who withdraw from the study early, Defined a completed subject, Corrected mild intermittent asthma to read intermittent asthma, Added and updated prohibited medications, including allowance for limited use of oral decongestants, Added information regarding weighing of nasal spray devices, Clarified the Visit 2 e-diary review required by clinical sites, Added information in Ophthalmic Examination section relating to ophthalmic solutions used by ophthalmologists when dilating subjects' eyes, Revised time period ophthalmologist has to send clinical investigator results of ophthalmic examinations, Clarified definition of 'family' history of cataract or glaucoma, Added a new section (Glucose Tests) to Clinical Laboratory Tests, Added information regarding the determination of subject compliance rate based on observed dosing via videophone, Added a reference, and Other minor administrative corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported