Clinical trial results:
Study FFU109045, A Comparison of Fluticasone Furoate Nasal Spray versus Oral Fexofenadine in the Treatment of Seasonal Allergic Rhinitis

Summary

EudraCT number	2015-004885-27
Trial protocol	Outside EU/EEA
Global end of trial date	28 February 2007

Results information

Result version number	v1 (current)
This version publication date	29 December 2016
First version publication date	29 December 2016

Trial information

Trial identification

Sponsor protocol code	FFU109045

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that Fluticasone furoate nasal spray (FFNS) provides superior nighttime symptom relief compared to fexofenadine as determined by the mean change from baseline in the nighttime nasal symptoms score (NSS)

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 2006
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: 936
Worldwide total number of subjects	936
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)	81
Adults (18-64 years)	831
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included 5-21 days of screening period followed by two weeks of treatment period and a Follow-up. Participants had to meet five symptom assessment criteria before randomization. Two of these were based on the average Nasal Symptom Score (NSS) assessment and three criteria's were based on the Daytime reflective Nasal Symptom Score D-rTNSS.

Pre-assignment

Screening details:

Total of 1360 participants were planned for enrollment so as to have 951 evaluable participants. A total of 1338 participants were screened and 936 were randomized.

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 vehicle placebo nasal spray and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.

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

Dosage and administration details:

Placebo nasal spray each morning once daily for two weeks following pre-dose symptom assessment.

Arm title	FFNS 110 microgram (mcg)

Arm description:

Participants received fluticasone fuorate nasal spray (FFNS) 110 mcg and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.

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

Dosage and administration details:

110 µg nasal spray each morning once daily for two weeks following pre-dose symptom assessment.

Arm title	Fex 180 milligram (mg)

Arm description:

Participants received oral capsule (overencapsulated fexofenadine [Fex] 180 mg oral tablet) and vehicle placebo nasal spray each morning once daily for two weeks following pre-dose symptom assessment.

Arm type	Active comparator
Investigational medicinal product name	Fexofenadine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Oral capsule (over encapsulated fexofenadine 180 mg oral tablet) each morning once daily for two weeks following pre-dose symptom assessment.

Number of subjects in period 1	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)
Started	313	312	311
Completed	290	298	287
Not completed	23	14	24
Randomized in error	1	-	-
Subject ended study one day early	1	-	-
Subject could not tolerate symptoms	-	-	1
Compliance less than 80 percent	1	-	-
subject could not swallow capsule	-	-	1
Visit changed to EarlyWithdrawn Visit	1	-	-
noncompliance with study requirements	1	1	1
Consent withdrawn by subject	1	-	2
Adverse event, non-fatal	1	2	6
Non-Compliance of diary	2	-	1
Pregnancy	2	-	-
In error, two study medications switched	1	-	-
Subject randomized with inadequate score	1	-	-
Subject moved eDiary and studymedication	1	-	-
Lost to follow-up	1	1	2
Protocol deviation	6	9	10
Lack of efficacy	2	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received vehicle placebo nasal spray and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.	
Reporting group title	FFNS 110 microgram (mcg)
Reporting group description:	
Participants received fluticasone fuorate nasal spray (FFNS) 110 mcg and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.	
Reporting group title	Fex 180 milligram (mg)
Reporting group description:	
Participants received oral capsule (overencapsulated fexofenadine [Fex] 180 mg oral tablet) and vehicle placebo nasal spray each morning once daily for two weeks following pre-dose symptom assessment.	

Reporting group values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)
Number of subjects	313	312	311
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	37.8	37.8	39.6
standard deviation	± 14.39	± 13.95	± 14.63
Gender categorical Units:			
Female	194	209	199
Male	119	103	112
Race, Customized Units: Subjects			
African American/African Heritage	22	26	9
American Indian or Alaska Native	7	5	6
Asian - Central/South Asian Heritage	3	1	1
Asian - East Asian Heritage	1	2	0
Asian - Japanese Heritage	0	1	0
Asian - South East Asian Heritage	2	1	2
Native Hawaiian or other Pacific Islander	2	1	2
White/Caucasian/European Heritage	270	268	286
Mixed Race	6	7	5

Reporting group values	Total		
Number of subjects	936		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	 -		
Gender categorical Units:			
Female	602		
Male	334		
Race, Customized Units: Subjects			
African American/African Heritage	57		
American Indian or Alaska Native	18		
Asian - Central/South Asian Heritage	5		
Asian - East Asian Heritage	3		
Asian - Japanese Heritage	1		
Asian - South East Asian Heritage	5		
Native Hawaiian or other Pacific Islander	5		
White/Caucasian/European Heritage	824		
Mixed Race	18		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received vehicle placebo nasal spray and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.	
Reporting group title	FFNS 110 microgram (mcg)
Reporting group description:	
Participants received fluticasone fuorate nasal spray (FFNS) 110 mcg and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.	
Reporting group title	Fex 180 milligram (mg)
Reporting group description:	
Participants received oral capsule (overencapsulated fexofenadine [Fex] 180 mg oral tablet) and vehicle placebo nasal spray each morning once daily for two weeks following pre-dose symptom assessment.	

Primary: Mean change from Baseline over the two-week treatment period in Nighttime Symptoms Score (NSS)

End point title	Mean change from Baseline over the two-week treatment period in Nighttime Symptoms Score (NSS)
End point description:	
The NSS is a three-item questionnaire which assesses three aspects of allergic rhinitis symptoms at night: (PM nasal congestion upon awakening [PMNCA], difficulty in going to sleep due to nasal symptoms [DSNS], and nighttime awakenings due to nasal symptoms [NANS]). These symptoms were rated using three 4-point scales, the sum of which comprises NSS. Each participant's baseline NSS was defined as the average of the NSS calculated for the day of randomization and the three highest NSS scores calculated during the six days immediately prior to the day of randomization. Each participant's average change from baseline NSS for Weeks 1-2 was the participant's average NSS over the treatment period minus the participant's baseline NSS. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).	
End point type	Primary
End point timeframe:	
Baseline and up to 2 weeks	

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[1]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
NSS, Week 1-2, n=312, 312, 309	-1.9 (± 0.1)	-2.9 (± 0.1)	-2 (± 0.09)	
PMNCA, Week 1-2, n=312, 312, 309	-0.6 (± 0.03)	-0.9 (± 0.03)	-0.6 (± 0.03)	
NANS, Week 1-2, n=312, 312, 309	-0.7 (± 0.04)	-1 (± 0.04)	-0.7 (± 0.03)	
DSNS, Week 1-2, n=312, 312, 309	-0.7 (± 0.04)	-1.1 (± 0.04)	-0.8 (± 0.04)	

Notes:

[1] - Intent To Treat (ITT) Population: Included all participants randomized to double-blind treatment.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.816
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Mean change from Baseline over the two-week treatment period in Nighttime Reflective Total Nasal Symptom Scores (N-rTNSS) and Component Nasal Symtoms Score

End point title	Mean change from Baseline over the two-week treatment period in Nighttime Reflective Total Nasal Symptom Scores (N-rTNSS) and Component Nasal Symtoms Score

End point description:

The nighttime reflective assessments were recorded each morning and assessed the four nasal symptoms (rhinorrhea, nasal congestion, nasal itching, and sneezing) over the previous 12 hours (evening and night). The scores of each of the four nighttime symptoms were summed for each participant to create a N-rTNSS for each day. Each participant's baseline total symptom score was the average of the nighttime total symptom score on the day of randomization and the three highest scores calculated for the six days immediately prior to the day of randomization. Each participant's average change from baseline nighttime total symptom score for Weeks 1-2 was the participant's average Nighttime total symptom score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[2]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TNSS, n=312, 312, 309	-2.5 (± 0.13)	-3.7 (± 0.14)	-2.7 (± 0.13)	
Nasal congestion, n=312, 312, 309	-0.6 (± 0.03)	-0.9 (± 0.04)	-0.7 (± 0.03)	
Itchy nose, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.7 (± 0.04)	
Runny nose, n=312, 312, 309	-0.6 (± 0.04)	-0.9 (± 0.04)	-0.7 (± 0.03)	
Sneezing, n=312, 312, 309	-0.7 (± 0.04)	-1 (± 0.04)	-0.7 (± 0.04)	

Notes:

[2] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)

Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.136
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.7

Variability estimate	Standard error of the mean
Dispersion value	0.18

Secondary: Mean change from Baseline over the two-week treatment period in Daytime Reflective Total Nasal Symptom Scores (D-rTNSS)

End point title	Mean change from Baseline over the two-week treatment period in Daytime Reflective Total Nasal Symptom Scores (D-rTNSS)

End point description:

The Daytime reflective assessments were recorded each evening and assessed the four nasal symptoms (rhinorrhea, nasal congestion, nasal itching, and sneezing) over the previous 12 hours (evening and night). The scores of each of the four Daytime symptoms were summed for each participant to create a D-rTNSS for each day. Each participant's baseline total symptom score was the average of the four highest total symptom score calculated for the seven days immediately prior to the day of randomization. Each participant's average change from baseline Daytime total symptom score for Weeks 1-2 was the participant's average Daytime total symptom score over the treatment period minus the participants baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[3]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TNSS n=312, 312, 309	-2.6 (± 0.13)	-3.7 (± 0.14)	-3 (± 0.13)	
Nasal congestion, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.03)	
Itchy nose, n=312, 312, 309	-0.7 (± 0.04)	-1 (± 0.04)	-0.8 (± 0.04)	
Runny nose, n=312, 312, 309	-0.6 (± 0.04)	-0.9 (± 0.04)	-0.7 (± 0.03)	
Sneezing, n=312, 312, 309	-0.7 (± 0.04)	-1.1 (± 0.04)	-0.9 (± 0.04)	

Notes:

[3] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.136
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.19

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.19

Secondary: Mean change from Baseline over the two-week treatment period in 24-hour Reflective Total Nasal Symptom Scores (24-hour rTNSS) and Component Nasal

Score.	
End point title	Mean change from Baseline over the two-week treatment period in 24-hour Reflective Total Nasal Symptom Scores (24-hour rTNSS) and Component Nasal Score.

End point description:

Daily 24-hour rTNSS was calculated as the average of the corresponding N-rTNSS and D-rTNSS. The 24-hour total symptom score for a Day is the average of the daytime total symptom score for that Day and the nighttime score for (D+1). If either component of a given date's 24-hour total symptom score was missing, then the 24-hour total symptom score itself were to be set to missing. Each participant's average change from baseline 24-hour total symptom score for Weeks 1-2 was the participants average 24-hour total symptom score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[4]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TNSS, n=312, 312, 308	-2.5 (± 0.13)	-3.6 (± 0.14)	-2.8 (± 0.13)	
Nasal congestion, n=312, 312, 308	-0.6 (± 0.03)	-0.9 (± 0.04)	-0.7 (± 0.03)	
Itchy nose, n=312, 312, 308	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Runny nose, n=312, 312, 308	-0.6 (± 0.03)	-0.9 (± 0.04)	-0.7 (± 0.03)	
Sneezing, n=312, 312, 308	-0.7 (± 0.04)	-1 (± 0.04)	-0.8 (± 0.04)	

Notes:

[4] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.136
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Secondary: Mean change from Baseline over the two-week treatment period in Nighttime Reflective Total Ocular Symptom Scores (N-rTOSS)

End point title	Mean change from Baseline over the two-week treatment period in Nighttime Reflective Total Ocular Symptom Scores (N-rTOSS)

End point description:

The nighttime reflective assessments were recorded each morning and assessed the three ocular symptoms (tearing/watering, itching/burning, and redness) over the previous 12 hours (evening and night). The scores of each of the three Nighttime symptoms were summed for each participant to create a N-rTOSS for each day. Each participants baseline total symptom score was the average of the nighttime total symptom score on the day of randomization and the three highest scores calculated for

the six days immediately prior to the day of randomization. Each participant's average change from baseline nighttime total symptom score for Weeks 1-2 was the participant's average Nighttime total symptom score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[5]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TOSS n=312, 312, 309	-2 (± 0.11)	-2.5 (± 0.11)	-2.2 (± 0.11)	
Eye tearing, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Eye itching, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Eye redness, n=312, 312, 309	-0.6 (± 0.04)	-0.8 (± 0.04)	-0.7 (± 0.04)	

Notes:

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)

Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.106
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.286
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Mean change from Bbaseline over the two-week treatment period in Daytime Reflective Total Ocular Symptom Scores (D-rTOSS)

End point title	Mean change from Bbaseline over the two-week treatment period in Daytime Reflective Total Ocular Symptom Scores (D-rTOSS)

End point description:

The Daytime reflective assessments were recorded each evening and assessed the three nasal symptoms (tearing/watering, itching/burning, and redness) over the previous 12 hours (evening and night). The scores of each of the three Daytime symptoms were summed for each participant to create a D-rTOSS for each day. Each participants baseline total symptom score was the average of the four highest total symptom score calculated for the seven days immediately prior to the day of randomization. Each participant's average change from baseline Daytime total symptom score for Weeks 1-2 was the participant's average Daytime total symptom score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:
Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[6]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TOSS n=312, 312, 309	-2.2 (± 0.11)	-2.6 (± 0.11)	-2.4 (± 0.11)	
Eye tearing, n=312, 312, 309	-0.8 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Eye itching, n=312, 312, 309	-0.8 (± 0.04)	-0.9 (± 0.04)	-0.9 (± 0.04)	
Eye redness, n=312, 312, 309	-0.7 (± 0.04)	-0.8 (± 0.04)	-0.7 (± 0.04)	

Notes:
[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.286
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.106
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Mean change from Baseline over the two-week treatment period in 24-hour Reflective Total Ocular Symptom Scores (24-hour rTOSS)

End point title	Mean change from Baseline over the two-week treatment period in 24-hour Reflective Total Ocular Symptom Scores (24-hour rTOSS)

End point description:

Daily 24-hour rTOSS was calculated as the average of the corresponding N-rTOSS and D-rTOSS. The 24-hour total symptom score for a Day is the average of the daytime total symptom score for that Day and the nighttime score for (D+1). If either component of a given date’s 24-hour total symptom score was missing, then the 24-hour total symptom score itself was to be set to missing. Each participant's average change from baseline 24-hour total symptom score for Weeks 1-2 was the participant's average 24-hour total symptom score over the treatment period minus the participant's baseline score. Baseline is the 4 highest scores calculated for the 7 days prior to Day 1. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[7]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
TOSS n=312, 312, 308	-2 (± 0.11)	-2.5 (± 0.11)	-2.2 (± 0.11)	
Eye tearing, n=312, 312, 308	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Eye itching, n=312, 312, 308	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Eye redness, n=312, 312, 308	-0.7 (± 0.04)	-0.8 (± 0.04)	-0.7 (± 0.04)	

Notes:

[7] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.286
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 2
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.106
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Mean change from Baseline over the two-week treatment period in Pre-dose Instantaneous Total Nasal Symptom Score (Pre-dose iTNSS) and Pre-dose Instantaneous Total Ocular Symptom Scores (Pre-dose iTOSS)

End point title	Mean change from Baseline over the two-week treatment period in Pre-dose Instantaneous Total Nasal Symptom Score (Pre-dose iTNSS) and Pre-dose Instantaneous Total Ocular Symptom Scores (Pre-dose iTOSS)

End point description:

Participants were instructed to score and document their symptoms in an instantaneous manner on a diary card. The instantaneous rating was performed once daily just prior to administering their morning dose. The scores of each of the three instantaneous nasal symptoms (nasal congestion, itching, rhinorrhea, and sneezing) and ocular symptoms (tearing/watering, itching/burning, and redness) were summed for each participant to create a iTNSS and iTOSS, respectively. Each participant's average change from Baseline iTNSS and iTOSS was the participant's average iTNSS and iTOSS total symptom score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[8]	312	311	
Units: Score on a scale				
arithmetic mean (standard error)				
TNSS, n=312, 312, 309	-2.3 (± 0.13)	-3.6 (± 0.14)	-2.6 (± 0.12)	
Pre-dose iTNSS, Nasal congestion n=312, 312, 309	-0.6 (± 0.03)	-0.8 (± 0.03)	-0.6 (± 0.03)	

Pre-dose iTNSS, Itchy nose n=312, 312, 309	-0.7 (± 0.04)	-1 (± 0.04)	-0.7 (± 0.04)	
Pre-dose iTNSS, Runny nose n=312, 312, 309	-0.6 (± 0.04)	-0.9 (± 0.04)	-0.6 (± 0.04)	
Pre-dose iTNSS, Sneezing n=312, 312, 309	-0.7 (± 0.04)	-1 (± 0.04)	-0.7 (± 0.04)	
TOSS, n=312, 312, 309	-1.9 (± 0.11)	-2.4 (± 0.12)	-2.2 (± 0.1)	
Pre-dose iTOSS, Eye tearing, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Pre-dose iTOSS, Eye itching, n=312, 312, 309	-0.7 (± 0.04)	-0.9 (± 0.04)	-0.8 (± 0.04)	
Pre-dose iTOSS, Eye redness, n=312, 312, 309	-0.6 (± 0.04)	-0.8 (± 0.04)	-0.7 (± 0.04)	

Notes:

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Pre-dose iTNSS	
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Pre-dose iTNSS	
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Pre-dose iTNSS	
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.193
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Pre-dose iTOSS	
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Pre-dose iTOSS	
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.058
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.15

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Pre-dose iTOSS	
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.16
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Mean change from Baseline over the two-week treatment period in Peak NasalIinspiratory Flow (PNIF)

End point title	Mean change from Baseline over the two-week treatment period in Peak NasalIinspiratory Flow (PNIF)

End point description:

PNIF was measured by participants using an In-Check Nasal portable hand-held inspiratory flow meter and face mask. Participants
recorded PNIF twice daily (in the morning prior to taking their study medication and in the evening). Three measurements were taken on each occasion and the highestmeasurement recorded on the electronic diary. Each participant's average change from Baseline PNIF was the participant's average PNIF over the treatment period minus the participant's baseline PNIF. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to 2 weeks

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[9]	312	311	
Units: Liter(L)/minute (min)				
arithmetic mean (standard error)				
Morning PNIF n=312, 312, 308	1.7 (± 0.99)	9.9 (± 1.28)	1.4 (± 1.18)	
Evening PNIF n=312, 311, 308	0.2 (± 1.12)	7.1 (± 1.31)	1.3 (± 1.23)	

Notes:

[9] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Morning assessment

Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	11.9
Variability estimate	Standard error of the mean
Dispersion value	1.59

Statistical analysis title	Statistical Analysis 2

Statistical analysis description: Morning assessment	
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	11.5
Variability estimate	Standard error of the mean
Dispersion value	1.59

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Morning assessment	
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.779
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	1.59

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Evening assessment	
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)

Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	9.6
Variability estimate	Standard error of the mean
Dispersion value	1.65

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Evening assessment	
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	10.3
Variability estimate	Standard error of the mean
Dispersion value	1.65

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Evening assessment	
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.662
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	4
Variability estimate	Standard error of the mean
Dispersion value	1.65

Secondary: Mean change from Baseline for Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ)

End point title	Mean change from Baseline for Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ)

End point description:

The NRQLQ is a paper instrument administered on the day of randomization and at Visit 4/Early Withdrawal to assess nocturnal rhinitis-related quality of life. The NRQLQ is a 16-item, self-administered, disease-specific (allergic rhinitis), and quality of life instrument that measures the functional problems most troublesome to patients with nocturnal allergy symptoms over a one-week interval. Each question is scored from 0 to 6 with higher scores indicating more nocturnal impairment. Items are grouped into four domains: Sleep problems, Sleep time problems, Symptoms on waking in the morning and Practical problems.An overall score was calculated from the mean score of all items. Each participant's average change from Baseline NRQLQ score was the participant's average NRQLQ score over the treatment period minus the participant's baseline score. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and Day 15

End point values	Placebo	FFNS 110 microgram (mcg)	Fex 180 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	313[10]	312	311	
Units: Scores on a scale				
arithmetic mean (standard error)				
Overall score, n=308, 309, 304	-1.3 (± 0.08)	-1.9 (± 0.09)	-1.5 (± 0.08)	
Sleep problems, n=308, 311, 305	-1.2 (± 0.09)	-1.9 (± 0.09)	-1.5 (± 0.09)	
Sleep time problems, n=308, 311, 305	-1.3 (± 0.09)	-1.9 (± 0.09)	-1.5 (± 0.09)	
Symptoms on waking, n=308, 309, 304	-1.4 (± 0.09)	-2 (± 0.1)	-1.5 (± 0.09)	
Practicle problems, n=308, 309, 304	-1.2 (± 0.09)	-1.9 (± 0.1)	-1.6 (± 0.1)	

Notes:

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	FFNS 110 microgram (mcg) v Fex 180 milligram (mg)

Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Fex 180 milligram (mg)
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.203
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v FFNS 110 microgram (mcg)
Number of subjects included in analysis	625
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.4

Variability estimate	Standard error of the mean
Dispersion value	0.11

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and Serious adverse events (SAEs) were collected from the time the first dose of study medication until the follow up contact (Up to Day 20)

Adverse event reporting additional description:

SAEs and non-serious AEs were collected in members of the Safety Population, comprised of all participants who received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received vehicle placebo nasal spray and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.

Reporting group title	Fex 180 milligram (mg)

Reporting group description:

Participants received oral capsule (overencapsulated fexofenadine [Fex] 180 mg oral tablet) and vehicle placebo nasal spray each morning once daily for two weeks following pre-dose symptom assessment.

Reporting group title	FFNS 110 microgram (mcg)

Reporting group description:

Participants received fluticasone fuorate nasal spray (FFNS) 110 mcg and oral placebo capsule each morning once daily for two weeks following pre-dose symptom assessment.

Serious adverse events	Placebo	Fex 180 milligram (mg)	FFNS 110 microgram (mcg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 313 (0.00%)	1 / 311 (0.32%)	0 / 312 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 313 (0.00%)	1 / 311 (0.32%)	0 / 312 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 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	Fex 180 milligram (mg)	FFNS 110 microgram (mcg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 313 (3.51%)	10 / 311 (3.22%)	12 / 312 (3.85%)
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 313 (3.51%)	10 / 311 (3.22%)	12 / 312 (3.85%)
occurrences (all)	13	11	14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2006	(1) permitted visit windows for Visits 3 and 4 that accommodated the Monday holidays which occurred during the study period, (2) permitted the use of the estrogenic vaginal ring as an acceptable method of birth control, and (3) provided a criterion for unacceptable diary compliance for the treatment period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported