



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicentre Study to Evaluate the Efficacy and Safety of Once-Daily Intranasal Administration of GW685698X Aqueous Nasal Spray 100mcg for 6 Weeks in Adult and Adolescent Subjects 12 years of Age and Older with Perennial Allergic Rhinitis (PAR)

Summary

EudraCT number	2005-004493-25
Trial protocol	LT EE LV DE
Global end of trial date	04 July 2006

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	20 June 2015

Trial information

Trial identification

Sponsor protocol code	FFR106080
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00289198
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)	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	11 August 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 July 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the efficacy and safety of GW685698X 100mcg QD aqueous nasal spray with vehicle placebo nasal spray in adult and adolescent subjects (12 years of age and older) with PAR.

Protection of trial subjects:

Participants were allowed to use short-acting inhaled beta2 agonists only on an as needed basis. Any clinically significant AE, laboratory test, nasal examination, ECG finding, or clinically significant unfavorable change observed during the Early Withdrawal Visit necessitated that the subject be followed or treated until satisfactory resolution occurred.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 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	Estonia: 34
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Latvia: 33
Country: Number of subjects enrolled	Lithuania: 36
Country: Number of subjects enrolled	Australia: 37
Country: Number of subjects enrolled	Canada: 66
Country: Number of subjects enrolled	New Zealand: 24
Country: Number of subjects enrolled	Russian Federation: 28
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	302
EEA total number of subjects	117

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)	39
Adults (18-64 years)	238
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Following a 7 to 14-day screening period, participants who met randomisation criteria were randomised to 6 weeks of treatment with fluticasone furoate (FF) or placebo nasal spray once daily (QD). A total of 302 participants were randomised, 151 in each of the treatment groups.

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 a blinded matching placebo aqueous nasal spray once daily (QD) every morning for 6 weeks. Dose was administered by alternately spraying one spray into each nostril followed by a second spray into each nostril for 42 days.

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 administer by alternately spraying one spray to each nostril followed by a second spray to each nostril (two sprays per nostril) once daily for 42 days

Arm title	FF 110 µg QD
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Arm description:

Participants received a blinded fluticasone furoate (FF) aqueous nasal spray 110 microgram (µg) QD every morning for 6 weeks. Dose was administered by alternately spraying one spray (27.5 µg per spray) into each nostril followed by a second spray into each nostril for 42 days.

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:

Self administer by alternately spraying one spray to each nostril followed by a second spray to each nostril (two sprays per nostril) once daily for 42 days. Each spray of the suspension will contain approximately 27.5 µg of GW685698X.

Number of subjects in period 1	Placebo	FF 110 µg QD
Started	151	151
Completed	120	121
Not completed	31	30
Consent withdrawn by subject	4	1
Physician decision	-	1
Low compliance	-	1
Adverse event, non-fatal	-	2
Impossible to come on schedule visit	-	1
Unable to attend on schedule	2	1
Miscalculation of visit date	21	22
Lack of efficacy	2	-
Protocol deviation	2	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a blinded matching placebo aqueous nasal spray once daily (QD) every morning for 6 weeks. Dose was administered by alternately spraying one spray into each nostril followed by a second spray into each nostril for 42 days.	
Reporting group title	FF 110 µg QD
Reporting group description:	
Participants received a blinded fluticasone furoate (FF) aqueous nasal spray 110 microgram (µg) QD every morning for 6 weeks. Dose was administered by alternately spraying one spray (27.5 µg per spray) into each nostril followed by a second spray into each nostril for 42 days.	

Reporting group values	Placebo	FF 110 µg QD	Total
Number of subjects	151	151	302
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	37.2 ± 16.2	37.1 ± 16.57	-
Gender categorical Units: Subjects			
Female	86	85	171
Male	65	66	131
Race, Customized Units: Subjects			
African American/African Heritage	3	4	7
American Indian or Alaska Native	1	0	1
Asian - Central/South Asian Heritage	1	2	3
Asian - East Asian Heritage	1	1	2
Asian - South East Asian Heritage	4	6	10
Native Hawaiian or other Pacific Islander	0	3	3
White - Arabic/North African Heritage	1	0	1
White - White/Caucasian/European Heritage	139	135	274
Mixed Race	1	0	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received a blinded matching placebo aqueous nasal spray once daily (QD) every morning for 6 weeks. Dose was administered by alternately spraying one spray into each nostril followed by a second spray into each nostril for 42 days.	
Reporting group title	FF 110 µg QD
Reporting group description: Participants received a blinded fluticasone furoate (FF) aqueous nasal spray 110 microgram (µg) QD every morning for 6 weeks. Dose was administered by alternately spraying one spray (27.5 µg per spray) into each nostril followed by a second spray into each nostril for 42 days.	

Primary: Mean change from Baseline (BL) in daily reflective total nasal symptom score (rTNSS) over the entire treatment period

End point title	Mean change from Baseline (BL) in daily reflective total nasal symptom score (rTNSS) over the entire treatment period
End point description: TNSS is the sum of symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing (each scored on a scale of 0 [none] to 3 [severe]; total possible score of 0 to 12). The rTNSS is a rating of the severity of symptoms over the previous 12 hours and is performed in morning (AM) and evening (PM). Daily rTNSS is defined as average of the PM rTNSS and the AM rTNSS of the next day prior to AM dosing. The BL daily rTNSS is defined as the average of the daily rTNSS over 4 consecutive 24-hour periods prior to randomization plus randomization day AM assessment. Change from BL was calculated as average of the non-missing daily rTNSS minus BL daily rTNSS. Analysis was performed using analysis of covariance (ANCOVA), adjusting for BL daily rTNSS, country, age, and gender. The Intent To Treat (ITT) Population comprised of all randomized participants who received ≥ 1 dose of study drug. Only those participants available at the specified time points were analyzed.	
End point type	Primary
End point timeframe: From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[1]	151 ^[2]		
Units: Scores on a scale				
least squares mean (standard error)	-2.69 (± 0.18)	-3.95 (± 0.18)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

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

Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.256
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	-0.78

Secondary: Mean change from Baseline in AM pre-dose instantaneous TNSS (iTNSS) over the entire treatment period

End point title	Mean change from Baseline in AM pre-dose instantaneous TNSS (iTNSS) over the entire treatment period
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End point description:

The AM pre-dose iTNSS is the sum of the 4 individual nasal symptom score assessments for rhinorrhea, nasal congestion, nasal itching, and sneezing performed at the moment immediately prior to taking the daily dose; each symptom is scored on a scale of 0 (none) to 3 (severe). Baseline iTNSS is defined as the average of the non-missing values for iTNSS during the Baseline period where the Baseline period included the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[3]	150 ^[4]		
Units: Scores on a scale				
least squares mean (standard error)	-2.36 (± 0.18)	-3.82 (± 0.18)		

Notes:

[3] - ITT Population

[4] - ITT Population

Statistical analyses

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

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.459
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.93
upper limit	-0.99

Secondary: Number of participants with response to therapy at Week 6

End point title	Number of participants with response to therapy at Week 6
End point description:	Response to therapy is defined as the effectiveness of FF for relieving allergic rhinitis symptoms over the entire treatment period. Response was, evaluated at the end of the study (Week 6) using a 7-point categorical scale, categorized as: 1=significantly improved, 2=moderately improved, 3=mildly improved, 4=no change, 5=mildly worse, 6=moderately worse, 7=significantly worse. Analysis was performed using logistic regression to evaluate treatment effect, adjusting for age, gender, and country.
End point type	Secondary
End point timeframe:	
Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151 ^[5]	151 ^[6]		
Units: Participants				
number (not applicable)				
Significantly improved	21	56		
Moderately Improved	38	37		
Mildly Improved	37	31		
No Change	45	20		
Mildly Worse	5	2		
Moderately Worse	3	3		
Significantly Worse	2	2		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

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

Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Logistic

Secondary: Mean change from Baseline in AM rTNSS over the entire treatment period

End point title	Mean change from Baseline in AM rTNSS over the entire treatment period
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End point description:

TNSS is the sum of symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing (each scored on a scale of 0 [none] to 3 [severe]; total possible score of 0 to 12). The AM rTNSS is a rating of the severity of symptoms performed in the morning prior to administering the dose of study drug and assesses how the participant felt during the night (preceding 12 hours). Baseline rTNSS is defined as the average of the non-missing values for rTNSS during the Baseline period where the Baseline period included the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[7]	150 ^[8]		
Units: Scores on a scale				
least squares mean (standard error)	-2.66 (± 0.17)	-3.93 (± 0.17)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.274
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	-0.81

Secondary: Mean change from Baseline in PM rTNSS over the entire treatment period

End point title	Mean change from Baseline in PM rTNSS over the entire treatment period
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End point description:

TNSS is the sum of symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing (each scored on a scale of 0 [none] to 3 [severe]; total possible score of 0 to 12). The PM rTNSS is a rating of the severity of symptoms performed approximately 12 hours after dosing and before bedtime and assesses how the participant felt during the day. Baseline rTNSS is defined as the average of the non-missing values for rTNSS during the Baseline period where the baseline period includes the 4 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[9]	150 ^[10]		
Units: Scores on a scale				
least squares mean (standard error)	-2.73 (± 0.18)	-4.02 (± 0.18)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.291
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.77
upper limit	-0.81

Secondary: Mean percent change from Baseline in Daily rTNSS over the entire treatment period

End point title	Mean percent change from Baseline in Daily rTNSS over the entire treatment period
End point description:	
TNSS is the sum of symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing (each scored on a scale of 0 [none] to 3 [severe]; total possible score of 0 to 12). The rTNSS is a rating of the severity of symptoms over the previous 12 hours and is performed in morning (AM) and evening (PM). Daily rTNSS is defined as average of the PM rTNSS and the AM rTNSS of the next day prior to AM dosing. The BL daily rTNSS is defined as the average of the daily rTNSS over 4 consecutive 24-hour periods prior to randomization plus randomization day AM assessment. Change from BL was calculated as average of the non-missing daily rTNSS minus BL daily rTNSS. Percentage change from BL was calculated as: (change from BL/BL)*100. Analysis was performed using ANCOVA, adjusting for BL daily rTNSS, country, age, and gender. Only those par. available at the specified time points were analyzed.	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[11]	151 ^[12]		
Units: Percentage of daily rTNSS				
least squares mean (standard error)	-30.23 (± 2.22)	-44.35 (± 2.21)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-14.118
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.03
upper limit	-8.21

Secondary: Mean percent change from Baseline in AM Pre-Dose iTNSS over the entire treatment period

End point title	Mean percent change from Baseline in AM Pre-Dose iTNSS over the entire treatment period
End point description:	
TNSS is the sum of symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing (each scored on a scale of 0 [none] to 3 [severe]; total possible score of 0 to 12). The AM pre-dose iTNSS is a	

rating of the severity of symptoms performed at the moment immediately prior to dosing. Baseline iTNSS is defined as the average of the non-missing values for iTNSS during the Baseline period where the Baseline period includes the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Percentage change from Baseline was calculated as: (change from Baseline/Baseline)*100. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[13]	150 ^[14]		
Units: Percentage of AM pre dose iTNSS				
least squares mean (standard error)	-24.67 (± 2.66)	-44.7 (± 2.66)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-20.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.13
upper limit	-12.94

Secondary: Mean change from Baseline in daily reflective individual nasal symptom scores (INSS) over the entire treatment period

End point title	Mean change from Baseline in daily reflective individual nasal symptom scores (INSS) over the entire treatment period
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End point description:

The individual nasal symptom scores (INSS) for rhinorrhea, nasal congestion, nasal itching and sneezing were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale and larger score indicates severe symptoms. The INSS is a rating of the severity of symptoms over the previous 12 hours and is performed in AM and PM. Daily INSS is defined as average of the PM INSS and the AM INSS of the next day prior to AM dosing. The BL daily INSS is defined as the average of the daily INSS over 4 consecutive 24-hour periods prior to randomization plus randomization day AM assessment. Change from BL was calculated as average of the non-missing daily INSS minus BL daily INSS. Analysis was performed using ANCOVA, adjusting for BL value, country, age, and gender. Only those par. available at the specified

time points were analyzed (n=X,X).

End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151 ^[15]	151 ^[16]		
Units: Scores on a scale				
least squares mean (standard error)				
Nasal congestion, n=150,151	-0.69 (± 0.05)	-0.97 (± 0.05)		
Nasal itching, n=150,151	-0.65 (± 0.05)	-0.98 (± 0.05)		
Sneezing, n=150,151	-0.68 (± 0.05)	-1.07 (± 0.05)		
Rhinorrhea, n=149, 150	-0.67 (± 0.05)	-0.94 (± 0.05)		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Daily rINSS for nasal congestion	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.14

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Daily rINSS for nasal itching	
Comparison groups	Placebo v FF 110 µg QD

Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.331
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.2

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Daily rINSS for sneezing	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.52
upper limit	-0.27

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Daily rINSS for rhinorrhea	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.277
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	-0.14

Secondary: Mean change from Baseline in AM pre-dose instantaneous individual nasal symptom score (iINSS) over the entire treatment period

End point title	Mean change from Baseline in AM pre-dose instantaneous individual nasal symptom score (iINSS) over the entire treatment period
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End point description:

iINSS for rhinorrhea, nasal congestion, nasal itching and sneezing were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale and larger score indicates severe symptoms. The AM pre-dose iINSS is a rating of the severity of symptoms performed at the moment immediately prior to dosing. Baseline iINSS is defined as the average of the non-missing values for iINSS during the Baseline period where the Baseline period included the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[17]	150 ^[18]		
Units: Scores on a scale				
least squares mean (standard error)				
Rhinorrhea	-0.57 (± 0.05)	-0.93 (± 0.05)		
Nasal Congestion	-0.55 (± 0.05)	-0.92 (± 0.05)		
Nasal Itching	-0.61 (± 0.05)	-0.98 (± 0.05)		
Sneezing	-0.63 (± 0.05)	-1 (± 0.05)		

Notes:

[17] - ITT Population

[18] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: AM pre-dose iINSS for rhinorrhea	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.357

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.22

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AM pre-dose iINSS for nasal congestion	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	-0.23

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AM pre-dose iINSS for nasal itching	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.372
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.24

Statistical analysis title	Statistical analysis 4
Statistical analysis description: AM pre-dose iINSS for sneezing	
Comparison groups	Placebo v FF 110 µg QD

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.372
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.24

Secondary: Mean change from Baseline in AM rINSS over the entire treatment period

End point title	Mean change from Baseline in AM rINSS over the entire treatment period
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End point description:

INSS for rhinorrhea, nasal congestion, nasal itching and sneezing were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale and larger score indicates severe symptoms. The AM rINSS is a rating of the severity of symptoms performed in the morning prior to administering the dose of study drug and assesses how the participant felt during the night (preceding 12 hours). Baseline rINSS is defined as the average of the non-missing values for rINSS during the Baseline period where the Baseline period included the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[19]	150 ^[20]		
Units: Scores on a scale				
least squares mean (standard error)				
Rhinorrhea	-0.67 (± 0.05)	-0.95 (± 0.05)		
Nasal Congestion	-0.66 (± 0.05)	-0.98 (± 0.05)		
Nasal Itching	-0.64 (± 0.05)	-0.96 (± 0.05)		
Sneezing	-0.69 (± 0.05)	-1.06 (± 0.05)		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

AM rINSS for rhinorrhea

Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.281
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.14

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AM rINSS for nasal congestion	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.314
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.17

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AM rINSS for nasal itching	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.324

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.19

Statistical analysis title	Statistical analysis 4
Statistical analysis description: AM rINSS for sneezing	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.374
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.25

Secondary: Mean change from Baseline in PM rINSS over the entire treatment period

End point title	Mean change from Baseline in PM rINSS over the entire treatment period
End point description: rINSS for rhinorrhea, nasal congestion, nasal itching and sneezing were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale and larger score indicates severe symptoms. The PM rINSS is a rating of the severity of symptoms performed approximately 12 hours after dosing and before bedtime and assesses how the participant felt during the day. Baseline rINSS is defined as the average of the non-missing values for rINSS during the Baseline period where the Baseline period included the 4 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.	
End point type	Secondary
End point timeframe: From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[21]	150 ^[22]		
Units: Scores on a scale				
least squares mean (standard error)				
Rhinorrhea	-0.66 (± 0.05)	-0.96 (± 0.05)		
Nasal congestion	-0.7 (± 0.05)	-0.97 (± 0.05)		
Nasal itching	-0.68 (± 0.05)	-1.01 (± 0.05)		
Sneezing	-0.68 (± 0.05)	-1.09 (± 0.05)		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: PM rINSS for rhinorrhea	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.292
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	-0.15

Statistical analysis title	Statistical analysis 2
Statistical analysis description: PM rINSS for nasal congestion	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.264
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	-0.12

Statistical analysis title	Statistical analysis 3
Statistical analysis description: PM rINSS for nasal itching	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.336
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	-0.2

Statistical analysis title	Statistical analysis 4
Statistical analysis description: PM rINSS for sneezing	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.412
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	-0.28

Secondary: Mean change from Baseline in daily reflective total ocular symptom score (rTOSS) over the entire treatment period

End point title	Mean change from Baseline in daily reflective total ocular symptom score (rTOSS) over the entire treatment period
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End point description:

TOSS is defined as the sum of the 3 individual ocular symptom scores for itching/burning eyes, tearing/watering eyes, and eye redness, and ranges from 0 to 9. Each symptom is scored on a 4 point (0 [none] to 3 [severe]) categorical scale. The rTOSS is a rating of the severity of symptoms over the previous 12 hours and is performed in AM and PM. Daily rTOSS is defined as average of the PM rTOSS and the AM rTOSS of the next day prior to AM dosing. The BL daily rTOSS is defined as the average of the daily rTOSS over 4 consecutive 24-hour periods prior to randomization plus randomization day AM

assessment. Change from BL was calculated as average of the non-missing daily rTOSS minus BL daily rTOSS. Analysis was performed using ANCOVA, adjusting for BL value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[23]	150 ^[24]		
Units: Scores on a scale				
least squares mean (standard error)	-1.41 (± 0.13)	-1.92 (± 0.13)		

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.506
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.16

Secondary: Mean change from Baseline in AM pre-dose instantaneous TOSS (iTOSS) over the entire treatment period

End point title	Mean change from Baseline in AM pre-dose instantaneous TOSS (iTOSS) over the entire treatment period
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End point description:

TOSS is defined as the sum of the 3 individual ocular symptom scores for itching/burning eyes, tearing/watering eyes, and eye redness, and ranges from 0 to 9. Each symptom is scored on a 4 point (0 [none] to 3 [severe]) categorical scale. The AM pre-dose iTOSS is a rating of the severity of symptoms performed at the moment immediately prior to dosing. Baseline iTOSS is defined as the average of the non-missing values for iTOSS during the Baseline period where the Baseline period included the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:
From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[25]	150 ^[26]		
Units: Scores on a scale				
least squares mean (standard error)	-1.26 (± 0.13)	-1.76 (± 0.13)		

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.491
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.13

Secondary: Mean Change from Baseline in AM rTOSS over the entire treatment period

End point title	Mean Change from Baseline in AM rTOSS over the entire treatment period
-----------------	--

End point description:

TOSS is defined as the sum of the 3 individual ocular symptom scores for itching/burning eyes, tearing/watering eyes, and eye redness, and ranges from 0 to 9. Each symptom is scored on a 4 point (0 [none] to 3 [severe]) categorical scale and larger score indicates more severe symptoms. The AM rTOSS is a rating of the severity of symptoms performed in the morning prior to administering the dose of study drug and assesses how the participant felt during the night (preceding 12 hours). Baseline rTOSS is defined as the average of the non-missing values for rTOSS during the Baseline period where the Baseline period includes the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[27]	150 ^[28]		
Units: Scores on a scale				
least squares mean (standard error)	-1.39 (± 0.13)	-1.92 (± 0.13)		

Notes:

[27] - ITT Population

[28] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.531
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	-0.19

Secondary: Mean change from Baseline in PM rTOSS over the entire treatment period

End point title	Mean change from Baseline in PM rTOSS over the entire treatment period
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End point description:

TOSS is defined as the sum of the 3 individual ocular symptom scores for itching/burning eyes, tearing/watering eyes, and eye redness, and ranges from 0 to 9. Each symptom is scored on a 4 point (0 [none] to 3 [severe]) categorical scale. The PM rTOSS is a rating of the severity of symptoms performed approximately 12 hours after dosing and before bedtime and assesses how the participant felt during the day. Baseline rTOSS is defined as the average of the non-missing values for rTOSS during the Baseline period where the baseline period includes the 4 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[29]	150 ^[30]		
Units: Scores on a scale				
least squares mean (standard error)	-1.44 (± 0.13)	-1.93 (± 0.13)		

Notes:

[29] - ITT Population

[30] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.496
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	-0.15

Secondary: Mean change from Baseline in daily reflective individual ocular symptom scores (IOSS) over the entire treatment period

End point title	Mean change from Baseline in daily reflective individual ocular symptom scores (IOSS) over the entire treatment period
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End point description:

individual ocular symptom scores (IOSS) for itching/burning eyes, tearing/watering eyes, and eye redness were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale. The IOSS is a rating of the severity of symptoms over the previous 12 hours and is performed in AM and PM. Daily IOSS is defined as average of the PM IOSS and the AM IOSS of the next day prior to AM dosing. The BL daily IOSS is defined as the average of the daily IOSS over 4 consecutive 24-hour periods prior to randomization plus randomization day AM assessment. Change from BL was calculated as average of the non-missing daily IOSS minus BL daily IOSS. Analysis was performed using ANCOVA, adjusting for BL value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[31]	151 ^[32]		
Units: Scores on a scale				
least squares mean (standard error)				
Eye itching/burning	-0.47 (± 0.05)	-0.69 (± 0.05)		
Eye tearing/watering	-0.48 (± 0.05)	-0.62 (± 0.05)		
Eye redness	-0.45 (± 0.04)	-0.61 (± 0.04)		

Notes:

[31] - ITT Population

[32] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: rIOSS for eye itching/burning	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.216
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	-0.09

Statistical analysis title	Statistical analysis 2
Statistical analysis description: rIOSS for eye tearing/watering	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.028
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.137
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.02

Statistical analysis title	Statistical analysis 3
Statistical analysis description: rIOSS for eye redness	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.156
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	-0.04

Secondary: Mean change from Baseline in AM Pre-Dose instantaneous individual ocular sumptom score (iIOSS) over the entire treatment period

End point title	Mean change from Baseline in AM Pre-Dose instantaneous individual ocular sumptom score (iIOSS) over the entire treatment period
End point description: IOSS for itching/burning eyes, tearing/watering eyes, and eye redness were assessed on a 4 point (0 [none]to 3 [severe]) categorical scale. The AM pre-dose iIOSS is a rating of the severity of symptoms performed at the moment immediately prior to dosing. Baseline iIOSS is defined as the average of the non-missing values for iIOSS during the Baseline period where the Baseline period includes the randomization day and the 3 consecutive days prior to randomization. Change from Baseline is calculated as the score over the entire treatment period minus the score at Baseline. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.	
End point type	Secondary
End point timeframe: From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[33]	150 ^[34]		
Units: Scores on a scale				
least squares mean (standard error)				
Eye itching/burning	-0.39 (± 0.05)	-0.6 (± 0.05)		
Eye tearing/watering	-0.43 (± 0.05)	-0.59 (± 0.05)		
Eye redness	-0.45 (± 0.05)	-0.56 (± 0.05)		

Notes:

[33] - ITT Population

[34] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: AM pre-dose iIOSS for eye itching/burning	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.215
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	-0.08

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AM pre-dose iIOSS for eye tearing/watering	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.016
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.161
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.03

Statistical analysis title	Statistical analysis 3
Statistical analysis description: AM pre-dose iIOSS for eye redness	
Comparison groups	Placebo v FF 110 µg QD

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.076
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.113
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.01

Secondary: Mean change from Baseline in AM reflective individual ocular symptom score (rIOSS) over the entire treatment period

End point title	Mean change from Baseline in AM reflective individual ocular symptom score (rIOSS) over the entire treatment period
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End point description:

rIOSS for itching/burning eyes, tearing/watering eyes, and eye redness were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale. The AM rIOSS is a rating of the severity of symptoms performed in the morning prior to administering the dose of study drug and assesses how the participant felt during the night (preceding 12 hours). Baseline rIOSS is defined as the average of the non-missing values for rIOSS during the Baseline period where the Baseline period includes the randomization day and the 3 consecutive days prior to randomization. Change from Baseline was calculated as score over the entire treatment period minus Baseline value. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[35]	150 ^[36]		
Units: Scores on a scale				
least squares mean (standard error)				
Eye itching/burning	-0.48 (± 0.05)	-0.69 (± 0.05)		
Eye tearing/watering	-0.48 (± 0.05)	-0.62 (± 0.05)		
Eye redness	-0.44 (± 0.05)	-0.61 (± 0.05)		

Notes:

[35] - ITT Population

[36] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

AM rIOSS for eye itching/burning

Comparison groups	Placebo v FF 110 µg QD
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Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.211
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	-0.08

Statistical analysis title	Statistical analysis 2
Statistical analysis description: AM rIOSS for eye tearing/watering	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.023
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.145
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	-0.02

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.176
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	-0.05

Secondary: Mean change from Baseline in PM rIOSS over the entire treatment period

End point title	Mean change from Baseline in PM rIOSS over the entire treatment period
End point description: IOSS for itching/burning eyes, tearing/watering eyes, and eye redness were assessed on a 4 point (0 [none] to 3 [severe]) categorical scale. The PM rIOSS is a rating of the severity of symptoms performed approximately 12 hours after dosing and before bedtime and assesses how the participant felt during the day. Baseline rIOSS is defined as the average of the non-missing values for rIOSS during the Baseline period where the baseline period includes the 4 consecutive days prior to randomization. Change from Baseline is calculated as the score over the entire treatment period minus the score at Baseline. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.	
End point type	Secondary
End point timeframe: From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[37]	150 ^[38]		
Units: Scores on a scale				
least squares mean (standard error)				
Eye itching/burning	-0.47 (± 0.05)	-0.69 (± 0.05)		
Eye tearing/watering	-0.49 (± 0.05)	-0.62 (± 0.05)		
Eye redness	-0.47 (± 0.05)	-0.61 (± 0.05)		

Notes:

[37] - ITT Population

[38] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: PM rIOSS for eye itching/burning	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.223
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	-0.09

Statistical analysis title	Statistical analysis 2
Statistical analysis description: PM rIOSS for eye tearing/watering	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.04
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	-0.01

Statistical analysis title	Statistical analysis 3
Statistical analysis description: PM rIOSS for eye redness	
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.022
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.142
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	-0.02

Secondary: Mean change from Baseline in daily peak nasal inspiratory flow (PNIF) over the entire treatment period

End point title	Mean change from Baseline in daily peak nasal inspiratory flow (PNIF) over the entire treatment period
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End point description:

PNIF is the tool for determining the extent of nasal airway obstruction. Participants used a portable hand-held inspiratory flow meter and face mask to measure and record PNIF. PNIF measurements were completed and recorded following assessment of allergy symptoms in the AM (prior to taking study medication), and 12 hours later in the PM (after recording allergy symptoms). Three measurements were taken and the highest measurement recorded on the electronic diary. Daily PNIF is defined as average of PM PNIF and AM PNIF of the next day prior to AM dosing. The BL is defined as average of the

last 8 readings (4 AM and 4 PM) of PNIF measurement over the four 24-hour periods prior to randomization. Change from Baseline is calculated as the value over the entire treatment period minus the value at Baseline. Analysis was performed using ANCOVA, adjusting for BL value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[39]	151 ^[40]		
Units: Liter per minute				
least squares mean (standard error)	17.35 (± 2.13)	25.72 (± 2.13)		

Notes:

[39] - ITT Population

[40] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.376
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.71
upper limit	14.04

Secondary: Mean change from Baseline in AM PNIF over the entire treatment period

End point title	Mean change from Baseline in AM PNIF over the entire treatment period
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End point description:

PNIF is the tool for determining the extent of nasal airway obstruction. Participants used a portable hand-held inspiratory flow meter and face mask to measure and record PNIF. AM PNIF measurements was completed and recorded following assessment of allergy symptoms in the AM (prior to taking study medication). Three measurements were taken and the highest measurement recorded on the electronic diary. Baseline AM PNIF is defined as the average of the non-missing values for PNIF during the Baseline period where the Baseline period includes the randomization day and the 3 consecutive days prior to randomization. Change from Baseline is calculated as the value over the entire treatment period minus the value at Baseline. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
End point timeframe:	
From Baseline up to Week 6	

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149 ^[41]	151 ^[42]		
Units: Liter per minute				
least squares mean (standard error)	16.33 (± 2.16)	25.61 (± 2.17)		

Notes:

[41] - ITT Population

[42] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.52
upper limit	15.04

Secondary: Mean change from Baseline in PM PNIF over the entire treatment period

End point title	Mean change from Baseline in PM PNIF over the entire treatment period
-----------------	---

End point description:

PNIF is the tool for determining the extent of nasal airway obstruction. Participants used a portable hand-held inspiratory flow meter and face mask to measure and record PNIF. PM PNIF measurements was completed and recorded after assessment of allergy symptoms in the PM (12 hours after study medication). Three measurements were taken on each occasion and the highest measurement recorded on the electronic diary. Baseline PM PNIF is defined as the average of the non-missing values for PNIF during the Baseline period where the Baseline period includes the 4 consecutive days prior to randomization. Change from baseline is calculated as the value over the entire treatment period minus the value at Baseline. Analysis was performed using ANCOVA, adjusting for Baseline value, country, age, and gender. Only those par. available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

From Baseline up to Week 6

End point values	Placebo	FF 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150 ^[43]	147 ^[44]		
Units: Liter per minute				
least squares mean (standard error)	18.51 (± 2.15)	26.15 (± 2.2)		

Notes:

[43] - ITT Population

[44] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v FF 110 µg QD
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.009
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.638
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	13.39

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study treatment until follow-up period (Up to 48 days).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the ITT population, comprised of all participants who were randomised to treatment, and received at least one dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants received a blinded matching placebo aqueous nasal spray once daily (QD) every morning for 6 weeks. Dose was administered by alternately spraying one spray into each nostril followed by a second spray into each nostril for 42 days.

Reporting group title	FF 110 µg QD
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Reporting group description:

Participants received a blinded fluticasone furoate (FF) aqueous nasal spray 110 microgram (µg) QD every morning for 6 weeks. Dose was administered by alternately spraying one spray (27.5 µg per spray) into each nostril followed by a second spray into each nostril for 42 days.

Serious adverse events	Placebo	FF 110 µg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 151 (0.66%)	
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: 2 %

Non-serious adverse events	Placebo	FF 110 µg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 151 (31.79%)	57 / 151 (37.75%)	
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	1 / 151 (0.66%) 1	4 / 151 (2.65%) 4	
Headache subjects affected / exposed occurrences (all)	29 / 151 (19.21%) 49	27 / 151 (17.88%) 46	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 151 (0.66%) 1	4 / 151 (2.65%) 4	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	5 / 151 (3.31%) 5	2 / 151 (1.32%) 3	
Epistaxis subjects affected / exposed occurrences (all)	6 / 151 (3.97%) 7	13 / 151 (8.61%) 20	
Nasal septum ulceration subjects affected / exposed occurrences (all)	0 / 151 (0.00%) 0	4 / 151 (2.65%) 5	
Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	6 / 151 (3.97%) 9	13 / 151 (8.61%) 16	
Skin and subcutaneous tissue disorders Scab subjects affected / exposed occurrences (all)	1 / 151 (0.66%) 1	4 / 151 (2.65%) 4	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 151 (4.64%) 10	9 / 151 (5.96%) 9	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 151 (3.97%) 6	3 / 151 (1.99%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 November 2005	removed the use of an Independent Data Monitoring Committee in this study, which has been included in error in the original protocol
14 February 2006	allowed the collection of nasal cytology samples at Early Withdrawal Visits (US and Canada only), added a requirement for subjects to be 18 years of age or older at Visit 1 (Germany only), corrected typographical errors on the cover sheet of Amendment 1, and made other minor text corrections in the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported