



## Clinical trial results:

### **A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Once-Daily, Intranasal Administration of GW685698X Aqueous Nasal Spray 100mcg for 4 Weeks in Adult and Adolescent Subjects (12 years of age and older) with Vasomotor/Idiopathic Rhinitis**

#### **Summary**

EudraCT number	2004-004744-43
Trial protocol	NO CZ DE
Global end of trial date	09 February 2006

#### **Results information**

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	22 July 2015

#### **Trial information**

##### **Trial identification**

Sponsor protocol code	FFR30007
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##### **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:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	20 April 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 February 2006
Was the trial ended prematurely?	No

Notes:

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**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 100 mcg once daily (QD) aqueous nasal spray with vehicle placebo nasal spray in adult and adolescent subjects ( $\geq 12$  years of age) with vasomotor rhinitis (VMR)/idiopathic rhinitis (IR).

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects****Subjects enrolled per country**

Country: Number of subjects enrolled	Czech Republic: 43
Country: Number of subjects enrolled	Germany: 68
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	United States: 174
Worldwide total number of subjects	347
EEA total number of subjects	139

Notes:

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**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)	11
Adults (18-64 years)	300

From 65 to 84 years	36
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Males and females  $\geq 12$  years of age, diagnosed with vasomotor rhinitis (VMR) and meeting the symptom requirements entered a 7 to 14 days screening period. Following screening period, participants meeting specified symptom criteria received treatment of either fluticasone furoate or placebo in 1:1 ratio up to 4 weeks.

### 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
<b>Arm title</b>	Placebo

Arm description:

Participants were instructed to self administer two sprays of Placebo into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril.

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

Dosage and administration details:

2 sprays of matching placebo once daily in the morning for 4 weeks

<b>Arm title</b>	Fluticasone furoate 110 µg QD
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Arm description:

Participants were instructed to self administer two sprays of fluticasone furoate 110 micrograms (µg) into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril

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

Dosage and administration details:

2 sprays of 110 µg once daily in the morning for 4 weeks

<b>Number of subjects in period 1</b>	Placebo	Fluticasone furoate 110 µg QD
Started	173	174
Completed	168	165
Not completed	5	9
Consent withdrawn by subject	2	5
Adverse event, non-fatal	1	1
'Patient took two different treatments '	-	1
Lost to follow-up	1	2
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants were instructed to self administer two sprays of Placebo into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril.

Reporting group title	Fluticasone furoate 110 µg QD
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Reporting group description:

Participants were instructed to self administer two sprays of fluticasone furoate 110 micrograms (µg) into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril

Reporting group values	Placebo	Fluticasone furoate 110 µg QD	Total
Number of subjects	173	174	347
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	44 ± 14.72	43.8 ± 15.44	-
Gender categorical Units: Subjects			
Female	108	124	232
Male	65	50	115
Race Units: Subjects			
African American/African Heritage	7	6	13
Japanese/East Asian /South East Asian Heritage	1	0	1
White	164	167	331
American Indian or Alaska Native & White	1	0	1
Asian & White	0	1	1

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were instructed to self administer two sprays of Placebo into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril.	
Reporting group title	Fluticasone furoate 110 µg QD
Reporting group description:	
Participants were instructed to self administer two sprays of fluticasone furoate 110 micrograms (µg) into each nostril once daily (QD) in the morning (AM), following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril	

### Primary: Mean change from Baseline in daily reflective total nasal symptom scores (rTNSS)

End point title	Mean change from Baseline in daily reflective total nasal symptom scores (rTNSS)
End point description:	
The TNSS is the sum of the three individual symptom scores for rhinorrhoea, nasal congestion, and post-nasal drip where each symptom was scored on a scale of 0 (no symptoms) to 3 (severe symptoms). The rTNSS is a rating of the severity of symptoms over the previous 12 hours and was performed in the morning (AM rTNSS) and evening (PM rTNSS). The daily rTNSS is the average of the AM rTNSS and PM rTNSS assessments. The analysis method used for comparison of the two treatment groups was Analysis of Covariance adjusting for baseline rTNSS, country, age, and gender, in addition to treatment effect.. The baseline daily rTNSS was defined as the average of the daily rTNSS over the 4 consecutive 24-hour periods prior to randomization, including the assessment on the morning of randomization.. Change from Baseline was calculated as the on-treatment value minus the Baseline. Intent-to-Treat population comprised of all participants who are randomized and received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline and up to Week 4	

End point values	Placebo	Fluticasone furoate 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172 <sup>[1]</sup>	172 <sup>[2]</sup>		
Units: Score on a scale				
least squares mean (standard error)	-2.11 (± 0.15)	-2.01 (± 0.15)		

Notes:

[1] - Intent to Treat(ITT) population. Only participants present at the specified timepoint were analyzed.

[2] - Intent to Treat(ITT) population. Only participants present at the specified timepoint were analyzed.

### Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Placebo v Fluticasone furoate 110 µg QD

Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.604
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.094
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.45

### Secondary: Mean change from Baseline in morning (AM) pre-dose instantaneous total nasal symptom scores (iTNSS)

End point title	Mean change from Baseline in morning (AM) pre-dose instantaneous total nasal symptom scores (iTNSS)
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End point description:

The AM pre-dose iTNSS is the sum of the three individual nasal symptom score assessments for rhinorrhoea, nasal congestion and postnasal drip performed immediately prior to taking the daily dose, where each symptom was scored on a scale of 0 to 3 for severity of symptoms. The analysis method used for comparison of the two treatment groups was Analysis of Covariance (ANCOVA) adjusting for baseline iTNSS, country, age, and gender, in addition to treatment effect. The baseline daily rTNSS was defined as the average of the daily rTNSS over the 4 consecutive 24-hour periods prior to randomization, including the assessment on the morning of randomization.. Change from Baseline was calculated as the on-treatment value minus the Baseline value.

End point type	Secondary
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End point timeframe:

Baseline and up to Week 4

End point values	Placebo	Fluticasone furoate 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172 <sup>[3]</sup>	172 <sup>[4]</sup>		
Units: Score on a scale				
least squares mean (standard error)	-1.65 (± 0.14)	-1.59 (± 0.14)		

Notes:

[3] - ITT population. Only participants available at the specified timepoint were analyzed.

[4] - ITT population. Only participants available at the specified timepoint were analyzed.

### Statistical analyses

Statistical analysis title	Analysis 2
Comparison groups	Placebo v Fluticasone furoate 110 µg QD



Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.729
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.41

### Secondary: Number of participants based on overall evaluation of response to therapy

End point title	Number of participants based on overall evaluation of response to therapy
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End point description:

Participants evaluated effectiveness of study medication for relieving non-allergic rhinitis symptoms over the entire treatment period. The overall evaluation of response to therapy was based on a 7-point categorical scale where the participants rate their perception of the change or lack of change in their VMR symptoms at the end of the study. The 7 categories were: significantly improved, moderately improved, mildly improved, no change, mildly worse, moderately worse, and significantly worse.

End point type	Secondary
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End point timeframe:

Week 4 (Day 29) or Early Withdrawal

End point values	Placebo	Fluticasone furoate 110 µg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172 <sup>[5]</sup>	171 <sup>[6]</sup>		
Units: Participants				
Significantly Improved	20	28		
Moderately Improved	39	41		
Mildly Improved	42	43		
No Change	63	50		
Mildly Worse	3	4		
Moderately Worse	2	3		
Significantly Worse	3	2		

Notes:

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

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

### Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Placebo v Fluticasone furoate 110 µg QD

Number of subjects included in analysis	343
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064 <sup>[7]</sup>
Method	Regression, Logistic

Notes:

[7] - Overall evaluation of response to therapy was analyzed using logistic regression adjusting for age, gender, investigator, and treatment.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from on or after the randomization date (Up to Day 34).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	8.1

### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants were instructed to self administer two sprays of Placebo into each nostril QD in the AM, following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril.

Reporting group title	Fluticasone furoate 110 µg QD
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Reporting group description:

Participants were instructed to self administer two sprays of fluticasone furoate 110 µg into each nostril QD in the AM, following pre-dose symptom assessment. Administration of the dose was performed by alternately spraying one spray to each nostril followed by a second spray to each nostril

Serious adverse events	Placebo	Fluticasone furoate 110 µg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 173 (0.00%)	1 / 174 (0.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 173 (0.00%)	1 / 174 (0.57%)	
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	Fluticasone furoate 110 µg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 173 (21.97%)	42 / 174 (24.14%)	
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	16 / 173 (9.25%) 24	14 / 174 (8.05%) 19	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 173 (0.00%) 0	4 / 174 (2.30%) 5	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)  Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	5 / 173 (2.89%) 11  5 / 173 (2.89%) 6	12 / 174 (6.90%) 12  4 / 174 (2.30%) 4	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	4 / 173 (2.31%) 6	1 / 174 (0.57%) 1	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)  Upper respiratory tract infection subjects affected / exposed occurrences (all)	10 / 173 (5.78%) 12  4 / 173 (2.31%) 4	11 / 174 (6.32%) 14  1 / 174 (0.57%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2005	This amendment is country specific and applies to Canada, Norway, Germany and Czech Republic. The primary purpose of this amendment is to clarify Section 5.2.1. Inclusion Criteria, #3, Age. The age of subjects for the above mentioned countries will be $\geq 18$ years at Visit 2.
13 June 2005	<ol style="list-style-type: none"><li>1) delete the term 'idiopathic rhinitis' from the protocol</li><li>2) delete the phrase that VMR symptoms are worsened by respiratory irritants and amend the:</li><li>3) Trademarks not owned by GlaxoSmithKline table</li><li>4) Document number of the GW685698X Investigator's Brochure</li><li>5) Introduction/Background</li><li>6) Rationale</li><li>7) Inclusion Criteria</li><li>8) Randomization Criteria</li><li>9) Exclusion Criteria</li><li>10) The organization of Section 6</li><li>11) Screening Period (Visit 1) section</li><li>12) ECG Procedure</li><li>13) Nasal Cytology section</li><li>14) Prohibited Medications</li><li>15) Medical Devices section</li><li>16) References</li><li>17) Time and Events Table</li><li>18) Vasomotor Rhinitis Questionnaire</li></ol> <p>A Vasomotor Rhinitis Trigger Questionnaire has been added (Appendix 7).</p> <p>In addition, other minor protocol text clarifications were made.</p>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported