



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 |
|-----------------------|----------|

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 | 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:

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 (≥ 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:

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:

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 ≥ 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 |
| Arm title | 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

| | |
|------------------|-------------------------------|
| Arm title | Fluticasone furoate 110 µg QD |
|------------------|-------------------------------|

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

| Number of subjects in period 1 | 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 |
|-----------------------|---------|

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

| 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 ^[1] | 172 ^[2] | | |
| 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) |
| End point description: | |
| <p>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.</p> | |
| End point type | Secondary |
| 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 ^[3] | 172 ^[4] | | |
| 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 |
|-----------------|---|

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 |
|----------------|-----------|

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 ^[5] | 171 ^[6] | | |
| 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 ^[7] |
| 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 |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 8.1 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

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 |
|-----------------------|-------------------------------|

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 ≥ 18 years at Visit 2. |
| 13 June 2005 | <ol style="list-style-type: none">1) delete the term 'idiopathic rhinitis' from the protocol2) delete the phrase that VMR symptoms are worsened by respiratory irritants and amend the:3) Trademarks not owned by GlaxoSmithKline table4) Document number of the GW685698X Investigator's Brochure5) Introduction/Background6) Rationale7) Inclusion Criteria8) Randomization Criteria9) Exclusion Criteria10) The organization of Section 611) Screening Period (Visit 1) section12) ECG Procedure13) Nasal Cytology section14) Prohibited Medications15) Medical Devices section16) References17) Time and Events Table18) Vasomotor Rhinitis Questionnaire <p>A Vasomotor Rhinitis Trigger Questionnaire has been added (Appendix 7).</p> <p>In addition, other minor protocol text clarifications were made.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported