A randomized, double-blind, placebo controlled, parallel group, multi-centre, 2-week treatment study to evaluate the safety and efficacy of fluticasone furoate nasal spray (FFNS) 110 mcg, administered either once daily or twice daily, compared with placebo, as effective monotherapy in the treatment of uncomplicated acute rhinosinusitis (ARS) in adult and adolescent subjects 12 years of age and older.

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The objective of this study is to evaluate the safety and efficacy of two doses of FFNS (110 mcg once daily and 110 mcg twice daily) compared to placebo as monotherapy in the treatment of adult and adolescent subjects 12 years of age and older with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON35004

Source
ToetsingOnline

Brief title
FFS113203

Condition

- Respiratory tract infections

Synonym
uncomplicated acute rhinosinusitis (ARS)

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline BV
Source(s) of monetary or material Support: Glaxosmithkline

Intervention

Keyword: corticosteroid, fluticasone, rhinosinusitis, uncomplicated

Outcome measures

Primary outcome

The primary efficacy endpoint for the study is the mean change from baseline in daily major symptom score (MSS) over the entire treatment period. The MSS is the sum of three individual symptom scores for (1) nasal congestion/stuffiness, (2) sinus headache/pressure or facial pain/pressure, and (3) postnasal drip that are rated by the subject using a 0 to 3 scale.

Secondary outcome

The key secondary endpoint is the first time to symptom improvement. Symptom improvement is defined as reduction of individual symptom scores of nasal congestion/stuffiness, sinus headache/pressure or facial pain/pressure, and postnasal drip to * 1 for 2 consecutive 12-hour assessments.

Other secondary endpoints will include the mean change from baseline over the entire treatment period in AM and PM MSS and daily, AM, and PM individual

symptom scores for nasal congestion/stuffiness, sinus headache/pressure or facial pain/pressure and postnasal drip, and the percentage of subjects who require the use of an antibiotic during the study due to the development of fulminant bacterial rhinosinusitis.

Health outcome measures include Sino-Nasal Outcome Test -20 (SNOT-20) and daily productivity and sleep diary questions.

Safety endpoints include adverse events, clinical laboratory tests, vital signs, and nasal examinations.

Study description

Background summary

Acute rhinosinusitis (ARS) is a condition caused by inflammation of the nose and the paranasal sinuses that generally lasts up to 4 weeks. Despite ARS being a self-limiting condition, untreated or inadequately treated sinus infection can lead to the development of complications. Uncomplicated ARS is a subset of ARS and is distinguished from the common cold by the persistence or the worsening of sinus inflammation after the usual period for recovery of viral infection of the nasal cavity (i.e., 10 days). Clinically the difference is based on the following criteria: symptoms are present at least 10 days but less than 4 weeks beyond the onset of upper respiratory symptoms OR symptoms worsen after 5 days from their onset. Uncomplicated ARS is further differentiated from fulminant bacterial rhinosinusitis by the absence of severe headache/facial/sinus pain and temperature > 38oC.
In the primary care settings, ARS is often treated empirically with antibiotics although they are shown to provide limited benefit in the uncomplicated ARS population. Alternatively, the use of an intranasal corticosteroid (INS) to control symptoms of uncomplicated ARS is plausible based on clinically proven ability to reduce inflammation and mucosal swelling. Indeed, data from recent studies in adults and adolescents have shown that the use of INS treatment as monotherapy or in conjunction with antibiotics provided efficacy in symptom reductions and improved recovery rates when treating ARS. Currently, only one INS, mometasone furoate, is approved in Canada for treating uncomplicated ARS as monotherapy, whereas there is no INS approved in Europe for this condition.
This study is a phase IIb dose finding study and one of two pivotal studies that will constitute the fluticasone furoate nasal spray (FFNS) global clinical

development program to support an indication for the treatment of uncomplicated ARS by FFNS. The optimal dose in treating uncomplicated ARS will be selected based on the results from this study and used for a subsequent confirmatory phase III study.

Study objective

The objective of this study is to evaluate the safety and efficacy of two doses of FFNS (110 mcg once daily and 110 mcg twice daily) compared to placebo as monotherapy in the treatment of adult and adolescent subjects 12 years of age and older with uncomplicated ARS.

Study design

This is a randomized, double-blind, placebo controlled, parallel group, multi-centre, 2-week treatment study. The study includes a 2-week post-treatment follow-up period.
Approximately 720 subjects will be randomized to one of three treatment groups for a period of 14 days: FFNS 110 mcg QD, FFNS 110 mcg BID, and placebo nasal spray. The randomization will be stratified by country, age (<18 years, >/=18 years), and allergic rhinitis (AR) status (Yes/No) based on documented skin prick test or in vitro blood test results.
Subjects who have ARS symptoms for 5-8 days will attend the study clinic for Visit 1 (screening visit) and subsequently enter 3 days of a screening period (with a permitted window of +2 days) during which they will record symptom scores twice daily (morning and evening) starting on the evening of Visit 1 and with the last assessment on the morning of Visit 2. Subjects who meet symptom requirements as well as other study entry criteria will be assigned to one of three study treatments at Visit 2 (Day 1) and start a 2-week study treatment. Subjects will attend the study clinic for Visits 3, 4 and 5 on Day 8 +/- 2 (end of 1-week treatment), Day 15 + 2 (end of 2-week treatment) and Day 22 +/- 2 (1-week post-treatment follow-up), respectively. Subjects will receive a follow-up telephone contact 7 days after Visit 5 to assess any post-treatment adverse events.

Intervention

Treatment with fluticasone furoate or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 5 visits and 1 telephone contact in 4 weeks.
Physical examination 2x, nasal examination 5x.
Blood tests safety 2x, total volume approx. 20 ml. Pharmacogenetic blood sample10 ml 1x (optional). Urine tests 2x. Allergy test (skin or blood) 0-1x.

Pregnancy test 3x. Questionnaire 3x. Diary (symptoms, use of study medication)
3 weeks.

Contacts

Public
GlaxoSmithKline BV

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Scientific
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Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age >= 12 years.
• Subject has provided an informed consent to participate. An appropriately signed and dated consent must be obtained from the parents or guardian of a subject who is under the legal age of consent.
• Diagnosis of uncomplicated acute rhinosinusitis
Subject has two or more major symptoms of uncomplicated acute rhinosinusitis [nasal

congestion/stuffiness, sinus headache/pressure or facial pain/pressure, and postnasal drip];
• One symptom must be sinus headache/pressure or facial pain/pressure; and
• Subject has experienced symptoms for at least 5 days and no more than 8 days prior to the screening visit (Visit 1).

Exclusion criteria

• Based on the investigator*s clinical judgement, subject has fulminant bacterial rhinosinusitis during the screening period including Visits 1 and 2.
• Acute rhinosinusitis in the past 12 weeks.
• Other sinonasal conditions in past 3 years.
• Allergic rhinitis.
• Influenza, candida-infection or ulcerations of the nose, otitis media.
• Obstructions like septumdeviation of polips.
• Antibiotica airway infections in the past 30 days.
• Use of analgecs (past 24 hours), corticosteroids (intranasal 4 weeks, others 8 weeks), other drugs infuencing nasal symptoms (detailed specification: see protocol).
• Swokers.
• Pregnancy and lactation.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-02-2010
Enrollment:	60

Type:	Actual

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-12-2009
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	30-12-2009
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	01-03-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	17-03-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam

(Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	Clinicaltrials.gov; registratienummer nog niet bekend.
EudraCT	EUCTR2009-015014-22-NL
CCMO	NL30481.003.09