An open label, part-randomised, four-way crossover, single and repeat dose study to determine the dose proportionality and absolute bioavailability of fluticasone furoate (FF) when administered as FF inhalation powder from the novel dry powder inhaler in healthy subjects.

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

Summary

ID

NL-OMON37181

Source
ToetsingOnline

Brief title
Four-way crossover, single and repeat dosing BA and BE study

Condition

- Respiratory tract infections

Synonym
chronic inflammation of the bronchial tubes; shortness of breath

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: asthma, bioavailability, proportionality

Outcome measures

Primary outcome

Pharmacokinetics: plasma drug concentrations

Safety: adverse events, physical examination if medically indicated

Secondary outcome

n/a

Study description

Background summary

Fluticasone furoate is a drug that may also be used for the treatment of asthma. Fluticasone furoate has not been registered for the treatment of asthma, however, in many countries including The Netherlands it has been registered for the treatment of chronic severe rhinitis. The drug has been administered extensively to asthma patients, COPD patients and healthy volunteers as part of the clinical development program. Fluticasone furoate is a corticosteroid, a chemical variant of a hormone produced by the body in the adrenal cortex which supresses various reactions during infection and inflammation.
In this study fluticasone furoate will be administered in a new form of inhalation, namely by an inhaler that contains the dry powder form of fluticasone furoate.

Study objective

The purpose of the study is to investigate to what extent blood concentrations of Fluticasone Furoate increase proportionately to rising doses of Fluticasone Furoate in three steps administered via a powder inhalator. In addition, the absolute bioavailability of the drug will be determined, i.e. drug concentrations reached in the blood following intravenous administration and inhalation of the drug will be compared.

Study design

A part-randomised, open-label, four-way cross-over single and repeat dose study in healthy male and female subjects.

Procedures and assessments:
Screening: Informed consent, demographics, medical history, clinical laboratory, full physical examination, ECG, vital signs, drug screen, HBsAg, anti HCV, anti-HIV 1/2, pregnancy test (females only), spirometry, inhaler practice.

Observation period: Period 1-3: in clinic from Day -1 up to 48 h after drug administration on Day 1; from Day 8 until 24 h after last drug administration on Day 9.
Period 4: from Day -1 up to 48 h after drug administration on Day 1

Blood sampling: for pharmacokinetics periods 1-4: Day 1: pre-dose, and several timepoints post-dose until 48 h post-dose.

Safety assessments: AE, SAE and concomitant medication review throughout the study; Brief physical exam: if deemend relevant; drugs of abuse; inhaler practice; vital signs; pregnancy test (females only)

Intervention

Treatment A
A single dose of 300mcg FF on Day 1, followed by 50mcg FF once daily for 7 days, on Days 3-9.
Treatment B
A single dose of 600 mcg FF on Day 1, followed by 100mcg FF once daily for 7 days, on Days 3-9.
Treatment C
A single dose of 1200mcg FF on Day 1, followed by 200mcg FF once daily for 7 days, on Days 3-9.
Treatment D
A single dose of 250mcg FF, administered as an IV infusion over 20 minutes on

Day 1.

Study burden and risks

Fluticasone Furoate Inhalation Powder: The study medicine is prepared with lactose (which contains milk protein). Allergic reactions may be seen when used in patients with a severe milk protein allergy or known hypersensitivity (medication allergy) to any ingredient of the medicine preparation. The study medicine also contains magnesium stearate, which is a substance commonly used in the manufacture of medical tablets and has no known side effects.
Side effects observed in previous studies with inhaled Fluticasone Furoate include:

Very common side effects (that occur in more than 1 in 10 patients)
* Headache
* Irritation and pain of the throat, nose and sinuses

Common side effects (that occur in more than 1 in 100 patients)
* Candidiasis (thrush) of the mouth and throat
* Upper Respiratory Tract Infections / Bronchitis
* Cough
* Loss of voice (Dysphonia)
* Fever (Pyrexia) and flu like symptoms
* Irritation and pain of the nose, throat and sinuses
* Pain and discomfort in the joints and back (Arthralgia)
* Abdominal pain

Rare side effects (that occur in less than 1 in 1,000 patients)
* Hypersensitivity reactions (allergic reactions)
* Abnormalities of heart rate (these were not serious and were seen during cardiac tests on patients)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy male or female
Between 18 and 65 years of age inclusive
BMI within the range 18.5-29.0 kg/m2 (inclusive).

Exclusion criteria

A positive pre-study Hepatitis B surface antigen or positive Hepatitis C antibody result within 3 months of screening.
A positive test for HIV antibody.
Where participation in the study would result in donation of blood or blood products in excess of 500 mL within a 56 day period.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-09-2012
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Fluticasone Furoate
Generic name:	not applicable
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-08-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2012-000614-11-NL
CCMO	NL41574.056.12