A PHASE 4, MULTINATIONAL, MULTICENTRE, DOUBLE BLIND, DOUBLE DUMMY, RANDOMIZED, PARALLEL GROUP, CONTROLLED CLINICAL STUDY OF FIXED COMBINATION BECLOMETHASONE DIPROPIONATE 100 µg PLUS FORMOTEROL FUMARATE 6 µg pMDI WITH HFA-134A PROPELLANT (CHF1535, FOSTER®) VERSUS FLUTICASONE 250 µg PLUS SALMETEROL 50 µg DPI (SERETIDE® DISKUS®) AS MAINTENANCE TREATMENT IN CONTROLLED ASTHMATIC PATIENTS

Published: 27-11-2008
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON33799

Source
ToetsingOnline

Brief title
FACTO study

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
asthma, lung inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Chiesi Farmaceutici
Source(s) of monetary or material Support: Chiesi Farmaceutici S.p.A.

Intervention

Keyword: CHF1535, controlled asthma patients, ICS/LABA fixed combination, Seretide

Outcome measures

Primary outcome

Pre-dose morning forced expiratory volume in one second (FEV1) measured at the

last clinic visit.

See page 42 from the protocol.

Secondary outcome

The following variables will be evaluated as secondary efficacy endpoints:

* Other pulmonary function tests measured at clinics (FEV1, PEF, FVC,

FEF25-75%);

* FEV1 area under the curve (AUC) in the first hour post-dose measured at

clinics at visit 2 and visit 5

* ACQ score at clinic visits 1, 2 (baseline) and 5

* Use of rescue medication;

* Number of patients with controlled or partly controlled asthma at clinic

visits according to GINA guidelines revised version 2007;

* Days without asthma symptoms (%), days without use of rescue medication (%)

and daily asthma symptoms* score from diary cards

* Pharmacoeconomic analyses assessing differences in direct medical costs

(healthcare perspective) and in both direct healthcare and indirect costs

(societal perspective).

See page 42 from the protocol.

Study description

Background summary

The management of asthma is currently focused on achieving optimal asthma control and reducing worsening of the disease. Combination therapies are often used to achieve this. At the moment, specific data aimed at assessing the clinical efficacy of CHF1535 in maintaining asthma control compared with other inhaled ICSs/LABAs fixed combinations are lacking.
Aim of the present investigation is to demonstrate the clinical equivalence between fluticasone plus salmeterol 500/100 µg daily and an equipotent dose of CHF1535 in maintaining the same asthma control in patients adequately controlled with fluticasone plus salmeterol at the above mentioned daily dose.
A pharmacoeconomic analysis will also be included.

Study objective

The objective of this study is to obtain information regarding the

effectiveness and safety of a product called Foster® for the treatment of asthma. This product is a combination between two well known drugs: formoterol fumarate and beclomethasone dipropionate and has been developed by the Italian Pharmaceutical Company Chiesi Farmaceutici S.p.A who is the sponsor of this study.
Primary objective:
To demonstrate the equivalence in terms of FEV1 between CHF1535 (beclometasone dipropionate plus formoterol fumarate, 400/24 µg daily) and an equipotent dose of Seretide® Diskus® (fluticasone propionate plus salmeterol, 500/100 µg / daily) in asthmatic patients already controlled on fluticasone plus salmeterol, 500/100 µg /daily.
Secondary objectives:
To evaluate the efficacy of the two treatment in terms of pulmonary function, use of rescue medications, maintenance of asthma control by GINA guidelines revised version 2007 (17) and Asthma Control Questionnaire (ACQ) (18), to evaluate the safety profile through adverse events (AEs) and adverse drug reactions (ADRs) reporting, 12-hour overnight urinary cortisol - creatinine ratio (OUCC), vital signs, and to assess treatment costs trough a cost minimisation analysis, comparing the total asthma-related direct medical costs in patients allocated to CHF1535 or to Seretide® Diskus.

Study design

A phase IV, multinational, multicentre, double-blind, double dummy, randomized, parallel group, controlled clinical study.

Intervention

This study will compare the effectiveness and safety of two active treatments in maintaining asthma control: this new product Foster® and a similar combination product on the market with a different corticosteroid fluticasone + another drug with bronchodilator effect salmeterol.

Study burden and risks

The study will last 16 weeks- 4 weeks run-in and 12 weeks treatment. The patients are under treatment with an active medication at all times.

Inconvenience:
During this period 5 visits will take place. At the beginning of each clinic visit a physical examination will be performed together with the measurement of vital signs. Vital signs will be measured before using study medication and after the last PFT.
During these visits any side effects from the study medication and any other medications being taken by the patient will be checked.

Lung function parameters (FEV1, FVC, PEF, FEF25-75%) will be measured before taking the first dose of study medication according to standardised procedures
During visits 1 and 5 the patients must come in a fasting condition (10 hours) for blood analysis.
During visits 2 and 5 FEV1 will also be assessed at 5, 15, 30 and 60 minutes after study drug administration.
During visits 1 and 5 a 12-lead electrocardiogram (ECG) will be performed.
During visits 2 and 5 a subgroup of 15% of patients will be asked to collect a 12-hour overnight urine sample to calculate the OUCC ratio.
On visits 1, 2 and 5 asthma control will be assessed according to GINA guidelines revised version 2007 and using the ACQ.
During the screening a urinary pregnancy test will be performed on women of a fertile age.
Patients will complete a diary card twice a day during the study.
Additional information will be collected for a pharmacoeconomic analysis.
Possible risks:

The inhalation of formoterol and salmeterol may sometimes cause side effects of a brief duration such as tremors (involuntary trembling or shaking) of the hands (usually temporary), related to the dose and disappearing with the treatment continuation), cephalgias(headache), palpitations(irregular, rapid beating or pulsation of the heart), tachycardia (excessively rapid heartbeat), skin allergy and muscular cramps.

The use of an inhaled corticosteroid such as beclomethasone and fluticasone might primarily induce local effects such as pharyngeal discomfort (discomfort in the area of the pharynx in the throat), dysphonia (speech disorder or voice disorders), and voice hoarseness indeed even a secondary event of a fungal infection of the throat. All these adverse effects can be prevented by rinsing the mouth with water after inhalation.

In subjects sensitive to the dry powder inhalation, a throat irritation with cough or hoarseness might appear; this can be avoided by rinsing the mouth out with water after the inhalation with fluticasone/salmeterol dry powder.
Allergic reactions such as nettle rash, itching sensations, skin rashes, and low blood pressure have also been reported.

The risks of this research are minimal as all medicines are registered and all patients are under treatment with and active medication at each moment of the study.

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

Written informed consent obtained from adult male or female (*18 and *65 years) patients with a clinical diagnosis of controlled asthma according to Global Strategy for Asthma Management and Prevention (GINA) revised version 2007 in the previous week before study entry (no daytime symptoms (twice or less/week):
- no limitations of activities
- no nocturnal symptoms/awakenings
- no need for reliever/rescue medications (twice or less/week)
- lung function (FEV1) > 80% predicted or personal best (if known), patients treated with fluticasone 500 µg + salmeterol 100 µg daily for * 4 weeks
A co-operative attitude and ability to correctly use the device and to complete the diary cards.

Exclusion criteria

Patients will not be enrolled at visit 1 into the run-in period if they meet any of the following

criteria:
1. Inability to carry out pulmonary function testing;
2. Diagnosis of Chronic Obstructive Pulmonary Disease (COPD) as defined by the National Heart Lung and Blood Institute/World Health Organisation (NHLBI/WHO) Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines;
3. History of near fatal asthma;
4. Evidence of severe asthma exacerbation or symptomatic infection of the lower airways in the previous six months;
5. Three or more courses of oral corticosteroids or hospitalisation due to asthma during the previous 6 months;
6. Patients treated with long-acting *2-agonists (LABAs) other than salmeterol, anticholinergics, and leukotriene antagonists during the previous 4 weeks;
7. Current smokers or recent (less than one year) ex-smokers defined as smoking at least 15 packs/year;
8. Clinically significant or unstable concurrent disease : e.g. uncontrolled hyperthyroidism, uncontrolled diabetes mellitus or other endocrine disease; significant hepatic impairment; significant renal impairment; significant other pulmonary disease; cardiovascular disease; gastrointestinal disease; neurological disease; haematological disease, autoimmune disorders, that may interfere with patient*s safety, compliance, or study evaluations, according to the investigator*s opinion;
9. Patients with a serum potassium value * 3.5 mEq/L
10. Patients with QTc interval (Bazett*s formula) higher than 450 msec at screening visit 1;
11. Cancer or any chronic diseases with prognosis < 2 years;
12. Female subjects: pregnant or with active desire to be pregnant, lactating mother or lack of efficient contraception in a subject with child-bearing potential (i.e. contraceptive methods other than oral contraceptives, IUD, tubal ligature). A pregnancy test in urine is to be carried out in women of a fertile age at screening
13. Significant alcohol consumption or drug abuse;
14. Patients treated with beta-blockers as regular use;
15. Patients treated with monoamine oxidase inhibitor, tricyclic antidepressants and Selective Serotonin Re-uptake Inhibitors (SSRIs), unless already taken at stable doses at the screening visit
16. Allergy, sensitivity or intolerance to study drugs and/or study drug formulation ingredients;
17. Patients unlikely to comply with the protocol or unable to understand the nature, scope and possible consequences of the study;
18. Patients who received any investigational new drug within the last 12 weeks;
19. Patients with asthma exacerbations during the run-in period will also be excluded from the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-05-2009
Enrollment:	110
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Foster
Generic name:	beclometason dipropionaat plus formoterol fumarate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Seretide
Generic name:	fluticasone plus salmeterol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ventolin
Generic name:	salbutamolsulfaat
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	27-11-2008

Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	20-02-2009
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	10-12-2009
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	07-07-2010
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2008-003740-11-NL
CCMO	NL25316.096.08