A DOUBLE BLIND, SINGLE DOSE, RANDOMIZED, 4-PERIOD CROSS-OVER, PLACEBO-CONTROLLED CLINICAL STUDY OF FIXED COMBINATION BECLOMETHASONE DIPROPIONATE PLUS FORMOTEROL FUMARATE (CHF 1535) VERSUS SINGLE AGENTS FORMOTEROL FUMARATE AND BECLOMETHASONE DIPROPIONATE VIA pMDI WITH HFA-134A PROPELLANT, WHEN GIVEN AFTER INHALED ALLERGEN CHALLENGE IN ASTHMATIC PATIENTS

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To investigate the effects of beclomethasone plus formoterol (in a single inhaler) versus single agents formoterol and beclomethasone dipropionate pMDI with HFA-134a propellant and placebo on the airway responses to allergen challenge. The primary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON32042

Source
ToetsingOnline

Brief title
MART3

Condition

- Bronchial disorders (excl neoplasms)

Synonym
allergic asthma, obstructive lung desease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Chiesi Farmaceutici,Chiesi Pharmaceuticals

Intervention

Keyword: allergen challenge, asthma, inflammation, pharmacotherapy

Outcome measures

Primary outcome

To demonstrate that CHF 1535 as single administration is superior to single components and to placebo in terms of late asthmatic response (LAR), when given after inhaled allergen challenge.

Secondary outcome

To assess the effects of the study drugs on early asthmatic response (EAR), airway hyperresponsiveness, induced sputum differential cell counts and inflammatory mediators in supernatant, fractional exhaled nitric oxide (FeNO) values and changes in VOCs behaviour.

Study description

Background summary

The management of asthma is currently focused on achieving optimal asthma control and reducing exacerbations. In mild asthma this can be achieved with ICS monotherapy, in moderate to severe persistent asthma with the addition of a (LABA: salmeterol or formoterol) to the ICS. Combination therapies are more convenient to use, control asthma at lower doses of ICS and ensure that the ICS are not discontinued when LABA is added. A new pharmacological approach is called SMART (Symbicort Maintenance and Reliever Therapy). The patient is taking a fixed dayly dose of the combination therapy for asthma control and an additional dose in response to symptoms. The most striking explanation at the basis of the SMART approach is that taking additional doses of the combination at the first signs of asthma worsening, it could be possible to extinguish airway inflammation at an early stage and prevent its evolution toward a more relevant inflammatory process into the airways leading to the clinical manifestations of exacerbation. This rationale is supported by recent evidences that asthma exacerbations are not rapid events, but evolve slowly over several days.

Study objective

To investigate the effects of beclomethasone plus formoterol (in a single inhaler) versus single agents formoterol and beclomethasone dipropionate pMDI with HFA-134a propellant and placebo on the airway responses to allergen challenge. The primary objective will be to demonstrate that CHF 1535 as single administration is superior to single components and to placebo in terms of late asthmatic response (LAR), when given after inhaled allergen challenge. The secondary objectives will be the assessment of study drugs on early asthmatic response (EAR), airway hyperresponsiveness, induced sputum differential cell counts, inflammatory mediators in supernatant, fractional exhaled nitric oxide (FeNO) values and volatile organic compounds detected with electronic nose.

Study design

Single centre, double blind, single dose, randomized, 4-period cross-over, placebo-controlled clinical study

Intervention

1. Foster (extrafine beclomethasone dipropionate 100 µg + formoterol fumarate 6 µg)
2. extrafine beclomethasone dipropionate 100 µg
3. formoterol fumarate 6 µg
4. placebo

Each patients recieves a single dose of each intervention (cross-over). The

treatment is given in four randomized, cross-over treatment periods, each composed of 3 consecutive days separated by 4 to 6 weeks of washout.

Study burden and risks

with each patient the following measurements will be performed:

14 x spirometry
1 x skin prick test
9 x methacholine/histamin challenge (PC20)
1 x ECG
11 x physical examination
1 x medical history
11 x vital signs
5 x allergenchallenge
16 x FeNO measurement
9 x electronic nose
8 x sputum induction
1 x blood sample

The patient will spend a total of 80 hours at the department.

The possible risks are:

- immediately after the inhalation of the allergen patients can have a reduction of the lung function, which will then carefully be monitored before and after the study drug administration and the symptoms will be adequately treated with adequate rescue medications and facilities.
The inhalation of formoterol may sometimes cause side effects of a brief duration such as tremors of the hands (usually transitory, related to the dose and disappearing with the treatment continuation), cephalgias, palpitations, tachycardia, skin allergy and muscular cramps.
The use of an inhaled corticosteroid such as beclomethasone might primarily induce local effects such as pharyngeal discomfort, dysphonia, voice hoarseness indeed even a secondary event of a fungal infection of the throat. All these adverse effects can be prevented by a rinsing of the mouth with water after inhalation.

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
- Male and female outpatients, aged * 18 years and * 55 years
- Clinical diagnosis of atopic controlled asthma for at least 6 months, according to Global Strategy for Asthma Management and Prevention (GINA) revised version 2006 Guidelines, without severe exacerbation in the previous 6 months before study entry
- Patients only taking short-acting *2-agonists on an as needed basis
- A provocative concentration of methacoline chloride or histamine causing a 20% fall in FEV1 (PC20) < 8 mg/ml
- A positive skin prick test (SPT) for house dust mite
- A documented EAR (* 20% fall in FEV1 from baseline, 0-3 h post allergen) and a LAR (* 15% fall in FEV1 from baseline, 3-8 h post-allergen) following inhaled allergen extract
- A co-operative attitude and ability to correctly use the device

Exclusion criteria

- Current smokers or recent (less than one year) ex-smokers
- Evidence of severe asthma exacerbation in the previous 6 months
- Clinically significant history of upper/lower respiratory tract infection within 4 weeks from

the start of the study
- 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, laboratory and electrocardiographic abnormalities that may interfere with patient*s safety, compliance, or study evaluations, according to the investigator*s opinion
- 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
- Patients treated with long-acting *2-agonists, anticholinergics and antihistamines and with topicalcorticosteroids and leukotriene antagonists during the previous 4 weeks
- Patients treated with beta-blockers in the week preceding the screening visit
- Patients who received systemic steroids in the previous 2 month
- Significant alcohol consumption or drug abuse
- Patients with allergy, sensitivity or intolerance to sympathomimetic drugs or corticosteroids or to any of the excipients contained in the study drugs
- Inability to perform spirometry of acceptable quality (according to ERS guidelines)or any other acute or chronic condition that put the patient at risk or may alter the interpretation of the test.
- Patients who received any investigational new drug or participated in clinical study within the previous 8 weeks before study entry

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2009
Enrollment:	20

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Atimos
Generic name:	formoterol fumarate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	CHF 718 HFA
Generic name:	beclometasone dipropionate
Product type:	Medicine
Brand name:	Foster
Generic name:	beclometasone dipropionate + formoterol fumarate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-04-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2008-002844-40-NL
CCMO	NL23421.058.08