A 12-week, multicentre, randomised, double-blind, double-dummy, 2-arm parallel group study comparing the efficacy and safety of Foster® 100/6 (beclomethasone dipropionate 100 µg plus formoterol 6 µg/actuation), 2 puffs b.i.d., versus Symbicort® 200/6 (budesonide 200 µg plus formoterol 6 µg/actuation), 2 inhalations b.i.d., on parameters of small airway function in patients with Chronic Obstructive Pulmonary Disease.

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Primary objective:To demonstrate the higher efficacy of small particles Foster® 100/6 (two puffs b.i.d.) versus large particles Symbicort® 200/6 (two inhalations b.i.d.), in terms of residual volume reduction in patients with chronic obstructive...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Pulmonary vascular disorders
Study type	Interventional

Summary

ID

NL-OMON38416

Source
ToetsingOnline

Brief title
FAIR

Condition

- Pulmonary vascular disorders

Synonym
chronic bronchitis, Lung of smoker

Research involving
Human

Sponsors and support

Primary sponsor: Chiesi Farmaceutici
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Chronic Obstructive Pulmonary Disease (COPD), Lung Diseases, Respiration Disorders

Outcome measures

Primary outcome

Primary efficacy variables

Change from baseline to end of treatment in post-dose residual volume.

Secondary outcome

Secondary efficacy variables

- Changes from baseline in FEV1, FVC, FEV1/FVC, IVC/FVC, RV, TLC, RV/TLC, FRC,

FRC/TLC, RV/VC, Raw, eff and sGaw, eff.

- Changes from baseline in airways resistance (R5, R20, R5-20) and reactance at

5 Hertz (X5) (in a subset of at least 50% of patients from pre-selected sites);

- Changes from baseline in COPD symptom scores (for each single score and the

total score);

- Change from baseline in percentage of COPD symptom-free days;

- Change from baseline in rescue salbutamol or ipratropium bromide consumption

(puffs per day);

- Change from baseline in percentage of rescue salbutamol or ipratropium

bromide-free days;

- Transition Dyspnoea Index (TDI) score at day 84 (V4);

- Clinical COPD Questionnaire (CCQ);

- Physical activity (by means of pedometer);

- Nasal brushing (mRNA expression);

- Number of patients with COPD exacerbations.

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is an incurable, debilitating and progressive disease that can be fatal. The recent Global Burden of Disease Study ranks COPD as the 6th leading cause of mortality and the 12th leading cause of morbidity world-wide. Furthermore, trends in the use of medical care resources indicate that the economic cost of COPD continues to rise in direct relation to the ageing population, the increase in prevalence of disease and the cost of new and existing medical and public health interventions.

The purpose of the present study is to demonstrate the higher efficacy of small particles Foster® 100/6 (two puffs b.i.d.) versus large particles Symbicort® 200/6 (two inhalations b.i.d.), in terms of residual volume reduction in patients with chronic obstructive pulmonary disease. In addition, we will evaluate the efficacy of the test treatments in terms of reduction of symptoms, improvements in health status (assessed by specific questionnaires) and in parameters related to the function of small airways in chronic obstructive pulmonary disease, and we will assess the safety.

Study objective

Primary objective:

To demonstrate the higher efficacy of small particles Foster® 100/6 (two puffs b.i.d.) versus large particles Symbicort® 200/6 (two inhalations b.i.d.), in terms of residual volume reduction in patients with chronic obstructive pulmonary disease.

Secondary objectives:
To evaluate the efficacy of the test treatments in terms of reduction of symptoms, improvements in health status (assessed by specific questionnaires) and in parameters related to the function of small airway function in patients with Chronic Obstructive Pulmonary Disease, and to assess the safety of study treatments.

Study design

This is a phase IIIb, multicentre, randomized, double-blind, double-dummy, 2-arm parallel group design preceded by a 4-week run-in period in 144 patients aged >= 40 years with COPD. The study will compare the efficacy and safety of Foster® 100/6 (two puffs b.i.d.) versus Symbicort® 200/6 (two inhalations b.i.d.), over a 12-week treatment period.
The study plan foresees:
-A pre-screening visit (V0, at week -5 before the randomization visit) during which clinical instructions to determine patients* adaptability to the study procedures will be performed. This can be done only after the participants have agreed to participate and have signed the Informed Consent form.
-A screening visit (V1, week -4) in which patients with COPD and lung hyperinflation will be selected.
-A 4-week run-in period where patients will receive a standardised treatment with Symbicort® Turbohaler® 200/6 µg, 1 inhalation b.i.d. (daily dose of BUD 400 µg plus FF 12 µg) and have any non-permitted medications withdrawn prior to entry into test treatment period.
-A randomisation visit (V2, week 0) during which patients will be allocated to one of the two treatment arms, and subsequent visits taking place at clinics after 4 weeks (V3) and after 12 weeks (V4) of treatment. After 8 weeks of treatment, a phone contact to document and treat adverse events occurred since the last visit, to record any change of concomitant medications being taken by the patient and to document any consumption of medical resources will be performed. The end of the trial is defined as the last visit of the last subject on the trial. After 7-10 days of last study medication intake, a follow-up phone contact to check the status of any adverse event which was still unresolved at the last visit will be performed.

Intervention

Treatment A: Foster® (beclomethasone dipropionate100 µg plus formoterol 6 µg), twice a day 2 puffs Foster®
twice a day 2 inhalations Symbicort ® Turbohaler® placebo

Treatment B: Symbicort® Turbohaler® (budesonide 200 µg plus formoterolfumarate 6 µg)
twice a day 2 puffs Foster® placebo
twice a day 2 inhalations Symbicort ® Turbohaler

Study burden and risks

All drugs may cause side effects. Beclomethasone dipropionate and formoterol are medicinal products that have been on the market for many years in many countries. The study medication Foster® is a combination similar to other combinations (Symbicort®, Seretide®) available on the market; therefore side effects associated with each of the compounds and similar to those reported for the other combinations may be expected.

Possible adverse effects are listed below, in order of their frequency of occurrence.

- Common (affecting less than 1 in 10 people):
Headache, hoarseness, sore throat.

- Uncommon (affecting less than 1 in 100 people):
- Palpitations, unusual fast heart beat and disorders of heart rhythm, some changes in the electrocardiogram (ECG).
- Flu symptoms, fungal infections (of the mouth and throat), fungal infections of the vagina, inflammation of the sinuses, rhinitis, inflammation of the ear, throat irritation, cough and productive cough, asthma attack.
- Nausea, abnormal or impaired sense of taste, burning of the lips, dry mouth, swallowing difficulties, indigestion, upset stomach, diarrhoea.
- Pain in muscle and muscle cramps, reddening of the face, increased blood flow to some tissues in the body, excessive sweating, trembling, restlessness, dizziness.
- Alterations of some constituents of the blood: fall in the number of white blood cells, increase in the number of blood platelets, a fall in the level of potassium in the blood, increase in blood sugar level, increase in the blood level of insulin, free fatty acid and ketones.

- Rare (affecting less than 1 in 1,000 people):
Feeling chest tightness, missed heartbeat (caused by too early contraction of the ventricles of the heart), increased or decrease in blood pressure, inflammation of the kidney, swelling of skin and mucous membrane persisting for several days, nettle rash or hives.

- Very rare (affecting less than 1 in 10,000 people):
Irregular heartbeat, shortness of breath, worsening of asthma, abnormal behaviour, sleep disorders and hallucinations, a fall in the number of blood platelets, swelling of the hands and feet.
There is a potential risk of unforeseeable allergic reactions as for any drug.

Hypersensitivity reactions like skin allergies, skin itching, skin rash, reddening of the skin, swelling of the skin or mucous membranes especially of the eyes, face, lips and throat may occur.
As with other inhaler treatments there is a risk of worsening shortness of breath and wheezing immediately after using (paradoxical bronchospasm).

Using high-dose inhaled corticosteroids over a long time can cause in very rare cases systemic effects: these include problems with how adrenal glands work (adrenosuppression), decrease in bone mineral density (thinning of the bones), growth retardation in children and adolescents, increased pressure in eyes (glaucoma), cataracts.

In case of any health problem related to the study the patient will immediately receive the adequate treatment.

In case the patient has to use salbutamol or ipratropium bronmide, which will be provided as a rescue medication during the study, the patient may possibly experience side effects associated with this drug: the most common are headache, dizziness, tremor, cough and local irritation. Occasionally, muscle cramps, tachycardia and palpitations.
The patient may experience minor discomfort from the blood sampling procedures, and occasionally some bruising or inflammation of the veins used for blood sampling. These effects normally disappear within a few days.

For female patients, there may be unknown risks to the foetus (unborn child). If the patient is a female patient of childbearing potential, the patient must not be pregnant and not intend to become pregnant during the whole study period. Women of childbearing potential have to use during their study participation and 30 days after a reliable method of contraception which will be: surgical sterilization (e.g. bilateral tubal ligation, hysterectomy), hormonal contraception (oral, implantable, patch, injectable), barrier methods [condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/cream/suppository)] or continuous abstinence (e.g. nuns). At visits 1 and visit 4, a blood pregnancy test is to be carried out if the patient a woman of a fertile age. As well breast feeding women are not allowed to participate in this study, because the study drug may enter the child*s body through the breast milk and cause harm. If a patient becomes pregnant in spite of precautions during the study period, the patient need to contact the study doctor instantly, who will withdraw the patient immediately from the study. Male patients must immediately inform the study doctor in case your partner becomes pregnant during your participation in the study

The patient will not be allowed to take some drugs: your study doctor will inform the patient about the medications not permitted during the study. In case of change of concomitant medications during the study, the patient must inform the study doctor beforehand.

The patient may not have participated in another trial with the study drugs (investigational drugs) in the 2 months prior to this study and must not participate in any other study for the time this one is ongoing.

The information obtained from this study may help us to propose in the future a new effective combination drug to the patients with COPD which is expected to have a positive effect on patient compliance (i.e., the patient adheres to the doctor*s instructions for treatment intake) to treatment and to improve the patient condition.
No matter which group the patient is assigned to, the patient will receive an active treatment for his disease which is expected to improve your lung functions. Moreover, the patient's disease and overall condition will be carefully and closely evaluated by the study doctor; this will help the doctor to assign you a more suitable drug therapy when the study is over (either by changing the dose of the drugs the patient was taking previously or by adding additional drug(s), etc.).

Contacts

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Chiesi Farmaceutici

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria
1. Male or female patients aged >= 40 years, who have signed an Informed Consent form prior to initiation of any study-related procedure or when applicable written informed consent obtained by legal representative.
2. Outpatients with a clinical diagnosis of severe to very severe COPD and including:
a) Smoking history of at least 10 pack years defined as [(number of cigarettes smoked per day) * (number of years of smoking)] / 20, both current and ex-smokers are eligible.
b) Regular use of bronchodilators (e.g. β2-agonist, anticholinergics) in the 2 months before visit 1.
c) Post-bronchodilator FEV1 < 50% of the predicted normal value at visit 1.
d) Post-bronchodilator FEV1/FVC < 0.7 at visit 1.
f) Plethysmographic Functional Residual Capacity (FRC) > 120% of the predicted normal value (at visit 1 and visit 2).
g) A Baseline Dyspnoea Index (BDI) focal score <=*10 (at visit 1 and at visit 2).
3. A cooperative attitude and ability to be trained to the proper use of pMDI and DPI (Turbohaler®, inspiratory flow-driven, multidose powder inhaler) inhalers.

Exclusion criteria

Exclusion criteria
1. Diagnosis of asthma or other clinically or functionally relevant respiratory disorders (other than COPD) which may interfere with data interpretation according to the investigator*s opinion.
2. Pregnant or lactating women. Females of childbearing potential without an efficient contraception UNLESS they meet the following definition of post-menopausal: 12 months of natural (spontaneous) amenorrhea or 6 months of spontaneous amenorrhea with serum FSH levels > 40 mIU/mL or are using one or more of the following acceptable methods of contraception:
a) surgical sterilization (e.g. bilateral tubal ligation, hysterectomy);
b) hormonal contraception (implantable, patch, oral, injectable);
c) barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/cream/suppository.
Reliable contraception should be maintained throughout the study and for 30 days after study drug discontinuation.
3. Clinically unstable concurrent disease: e.g. hyperthyroidism, diabetes mellitus or other endocrine disease; significant hepatic impairment; significant renal impairment; cardiovascular disease (e.g. coronary artery disease, hypertension, heart failure); gastrointestinal disease (e.g. active peptic ulcer); neurological disease; haematological

disease; autoimmune disorders, or other which may impact the evaluation of the results of the study according to investigator*s judgement.
4. Patient with narrow-angle glaucoma.
5. Clinically significant laboratory and ECG abnormalities indicating a significant or unstable concomitant disease which may impact the evaluation of the results of the study and the safety of the patient according to investigator*s judgement.
6. Patients with COPD exacerbation and/or symptomatic infection of the airways requiring antibiotic therapy (at least 5 days) in the 2 months prior to screening and during the study period. COPD exacerbation will be defined according to the following: *A sustained worsening of the patient*s condition (dyspnoea, cough and/or sputum production/purulence), from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD that includes prescriptions of systemic corticosteroids (at least 3 days) and/or antibiotics (at least 5 days), or need for a visit to an emergency department or hospitalization*.
7. Patients requiring long term (> 12 hours daily) oxygen therapy for chronic hypoxemia.
8. Patients treated with depot corticosteroids in the 2 months preceding the visit 1 and during the run-in period.
9. Patients with known allergy, sensitivity or intolerance to sympathomimetic drugs or inhaled corticosteroids or to any of the excipients contained in the study drugs.
10. Patients who have evidence of alcohol or drug abuse, not compliant with the study protocol or not compliant with the study treatments according to investigator*s judgement.
11. Major surgery in the previous 3 months and during the trial which may affect patient*s compliance in study procedures (e.g. plethysmography).
12. Participation in another clinical trial with an investigational drug in the 2 months preceding visit 1.
13. Patients requiring chronic mechanical ventilation for COPD.

Study design

Design

Study phase:	3
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):	30-09-2011
Enrollment:	170
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Foster®
Generic name:	formoterol fumarate 6 µg /beclomethasone dipropionate 100 µg
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-05-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-08-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2010-022895-30-NL
CCMO	NL36468.042.11