Effect of inhalation of tiotropium once daily 18 mcg versus salmeterol twice daily 50 mcg on time to first exacerbation in COPD patients (a randomized, double-blind, double-dummy, parallel group, one year study)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Upper respiratory tract disorders (excl infections)
Study type	Interventional

Summary

ID

NL-OMON31594

Source
ToetsingOnline

Brief title
POET

Condition

- Upper respiratory tract disorders (excl infections)

Synonym
dyspnoe, pulmonary disease

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim

Intervention

Keyword: COPD, Exacerbation, Salmeterol, Tiotropium

Outcome measures

Primary outcome

The Primary Endpoint is the time to first COPD exacerbation

Secondary outcome

The Secondary Endpoints are:

1. Occurrence of at least one exacerbation

2. Number of COPD exacerbations

3. Time to first hospitalisation due to COPD exacerbation

4. Occurrence of at least one hospitalization due to COPD exacerbations

5. Number of hospitalisations due to COPD exacerbations

6. Time to premature discontinuation of trial medication

7. Occurrence of premature discontinuation of trial medication

8. Pre-dose morning PEFR measured by patients at home during the first four

months of randomised treatment (weekly means will be calculated)

9. Time to first COPD exacerbation or time to discontinuation of study

medication because of worsening of underlying disease, whichever comes first

Study description

Background summary

Several drug therapies have been shown to reduce exacerbations. Inhaled long-acting ß2-agonists such as salmeterol and formoterol have somewhat conflicting data regarding effects on exacerbations while the long-acting anticholinergic tiotropium appears to consistently reduce exacerbation rates [P99-01272, P03-01576, P03-01593, P04-00293, P05-09172, R07-0368]. Nevertheless, both are recommended in international guidelines for the treatment of COPD as maintenance therapy [P05-12781]. In clinical trials, tiotropium has been shown to improve lung function, health-related quality of life, dyspnoea, exercise tolerance and to prevent exacerbations [P02-01288, P02-01290, P03-04061, P04-1571]. However, it is still unclear whether tiotropium can be demonstrated in a randomized, blinded clinical trial to be more effective in reducing exacerbations compared with long-acting ß2-agonists such as salmeterol.

Study objective

To demonstrate superiority of tiotropium vs. salmeterol in reducing exacerbations which are an important patient outcome because they are a major cause of morbidity from COPD. In addition, they are associated with a more rapid decline in lung function over time and contribute to decline of health-related quality of life

Study design

One year randomized, double-blind, double-dummy, parallel group design. Study consists of 6 visits (Screening, study start, 2, 4, 8 and 12 months) and 8 telephone calls monthly between the visits. Patients randomized by IVRS into 2 groups: tiotropium 18 mcg once daily via the HandiHaler® + placebo MDI twice daily or salmeterol 50 mcg twice daily + placebo capsules once daily via the HandiHaler®.

Pharmacogenetic sub-study: Participation is voluntary and is not a prerequisite for participation in the study. One blood sample will be taken from patients who have signed separate informed consent.

Intervention

Subjects will be randomly assigned to 1 of 2 treatment groups: tiotropium 18 mcg once daily via the HandiHaler® + placebo MDI twice daily or salmeterol 50 mcg twice daily + placebo capsules once daily via the HandiHaler®. Subjects who are at screening treated with tiotropium will be switched to

ipatropium first due to the long elimination half-life of tiotropium.

Study burden and risks

Tiotropium is indicated as a maintenance bronchodilator treatment to relieve symptoms of patients with chronic obstructive pulmonary disease (COPD) [see SPC].
Salmeterol is a selective β2-agonist indicated for reversible airways obstruction in patients with asthma and chronic obstructive pulmonary disease (COPD) [see SPC].
In the present clinical trial, both medications will be studied within their approved indications.

Safety evaluations:
1. Serious adverse events
2. Adverse events leading to treatment discontinuation
3. All-cause mortality during treatment with study medication
4. All-cause mortality including follow-up of vital status from patients who prematurely discontinue treatment
5. Physical examination

Health economic analysis: For the purpose of a separate health economic analysis (for example cost-effectiveness analysis including the clinical endpoint as the effectiveness parameter), health care resource utilization (HCRU) data will be collected.

Pharmacogenetic sub-study: Participation is voluntary and is not a prerequisite for participation in the study. One blood sample will be taken from patients who have signed separate informed consent.

Contacts

Public
Boehringer Ingelheim

Binger Strasse 173
55218 Ingelheim
Duitsland
Scientific
Boehringer Ingelheim

Binger Strasse 173
55218 Ingelheim
Duitsland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Current or ex-smoker, 40 years of age or older, diagnosed with COPD with at least one exacerbation within the past year requiring treatment.
Patients must have a post-bronchodilator FEV1 <= 70% of predicted normal and FEV1 <= 70% of FVC post-bronchodilator.

Exclusion criteria

Patients with cardiac-related conditions, significant diseases other than COPD and other concomitant conditions and therapies that will have an impact on the wellbeing of the patient or may influence either the result of the study or the patients' ability to participate in 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):	10-03-2008
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	serevent
Generic name:	salmeterol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	spiriva
Generic name:	tiotropium
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	12-11-2007
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

Approved WMO

Date:	29-11-2007
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

Approved WMO

Date:	05-03-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

Approved WMO Date:	13-03-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	24-04-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	17-06-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	20-06-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	15-12-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	13-01-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	09-10-2009
Application type:	Amendment

Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	15-10-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	15-12-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	01-02-2010
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	09-02-2010
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
EudraCT	EUCTR2007-001840-33-NL
CCMO	NL20013.003.07