A randomized, double-blind, controlled, parallel group, 12-week treatment study to compare the efficacy and safety of the combination of indacaterol 150 µg once daily with open label tiotropium 18 µg once daily versus open label tiotropium 18 µg once daily in patients with moderate-to-severe chronic obstructive pulmonary disease.

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To demonstrate the superiority of indacaterol 150 µg o.d. in combination with tiotropium 18 µg o.d. versus tiotropium 18 µg o.d. with respect to standardized area under the curve (AUC) for forced expiratory volume in 1 second (FEV1) between 5 min *...

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

Summary

ID

NL-OMON33827

Source
ToetsingOnline

Brief title
CQAB149B2351

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Chronic Obstructive Pulmonary Disease, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: De industrie;opdrachtgever Novartis Pharma BV.

Intervention

Keyword: Bronchodilation, COPD, Indacaterol, Tiotropium

Outcome measures

Primary outcome

Standardized area under the curve (AUC) between 5 min and 8 h post-dose for

forced expiratory volume in 1 second (FEV1) after 12 weeks of treatment.

Secondary outcome

Efficacy

Key: 24 hour post-dose trough FEV1 after 12 weeks of treatment. The 24 h

post-dose trough FEV1 is defined as the avarage of FEV1 measurements at 23 h 10

min and 23 h 45 min post-dose.

Other: Standardized AUC 5min-8h FEV1 on Day 1, Standardized AUC 5min-4h FEV1 on

Day 1 and after 12 weeks treatment,

Trough FEV1 on Day 2, FEV1 and FVC at individual time points, Peak FEV1 during

4 h post dose, Inspiratory Capacity, Symptom scores over 12 weeks, Daily Rescue Medication use (number of puffs) over 12 weeks, Daily rescue medication use (number of puffs) at 4 weekly intervals, Percentage of *days with no rescue use* over 12 weeks.

Safety

Adverse events, ECG and vital signs, laboratory data

Study description

Background summary

This study will provide 12 weeks of comparative efficacy and safety data on indacaterol (150 µg o.d.) combined with tiotropium (18 µg o.d.) versus tiotropium (18 µg o.d.) alone. This data will support GOLD guidelines recommendations that suggest combining two bronchodilators with complementary actions on airways may increase and sustain bronchodilation in patients with chronic obstructive pulmonary disease (COPD).

Study objective

To demonstrate the superiority of indacaterol 150 µg o.d. in combination with tiotropium 18 µg o.d. versus tiotropium 18 µg o.d. with respect to standardized area under the curve (AUC) for forced expiratory volume in 1 second (FEV1) between 5 min * 8 h post-dose after 12 weeks of treatment in patients with moderate-to-severe COPD.

Study design

This is a 12 week, multicenter, randomized, double-blind, controlled, parallel group study. At the pre-screening Visit 1 informed consent is obtained and current COPD medications are reviewed and adjusted if necessary (washout period of approximately one week). Then begins a screening/run-in period of 14 days. Patients whose elegibility is confirmed after the screening/run-in period will

be randomized to one of two treatment groups using an allocation ratio of 1:1. The randomization will be stratified by COPD severity (moderate or severe, as classified by the GOLD Guidelines, 2007).

Intervention

Patients will be assigned to one of the following 2 treatment arms in a ratio of 1:1
1. Indacaterol 150 µg o.d. + open label tiotropium 18µg o.d.
2. Placebo to indacaterol + open label tiotropium 18µg o.d.

At visit 1 all patients will be provided with salbutamol which they will be instructed to use throughout the study as rescue medication.

Study burden and risks

Burden:
The patient will be asked to come to the clinic for a visit 9 times over about 15 weeks and take two capsules study medication once a day for 12 treatment weeks. The study medication is inhaled by using a different inhaler for each capsule. A serum pregnancy test will be done 2x (when applicable), 2x a physical exam, at 3 visits ECGs will be made (in total 11x), at 7 visits bloodpressure and pulse rate are measured (in total 9x), at 3 visits urine is tested, at 3 visits blood samples are taken (in total at 5 timepoints), at 8 visits long function tests are done including 2x a reversibility test and at 2 days measurements up to 8 hours postdose (in total 28x). Furthermore, the patient will be asked to complete an electronic diary twice daily.

Risks:
Possible side effects of the study medicine indacaterol (QAB149) can include: tremor, headache, cough, post-inhalation cough, palpitations, muscle cramps, nausea, chest pain, trouble sleeping, nervousness, dry mouth, dizziness, tiredness, feeling generally unwell and possible changes in blood pressue or potassium or blood sugar.
Side effects of the other study medicine, tiotropium (Spiriva®), include: dry mouth, constipation, tremor, headache, palpitations, blurred vision, glaucoma, urinary difficulty, urinary retention, muscle cramps and nausea.
Unexpected problems or side effects that are not known could also occur.
Taking blood and measuring blood pressure could be unpleasant. The risks of taking blood may include fainting, pain and/or bruising. Rarely, these may be a small blood clot or infection at the site of the needle puncture. In rare instances where a nurse, a doctor, or laboratory technician, sustains an exposure to a patients blood, it may be necessary to test the blood for Hepatitis-B, Hepatitis-C and HIV.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male and female adults aged 40 years and over
2. Co-operative outpatients with a diagnosis of COPD (moderate to severe as classified by the GOLD Guidelines, 2007) and including:
a) Smoking history of at least 10 pack years, both current and ex-smokers are eligible
b) Post-bronchodilator FEV1 * 65% and * 30% of the predicted normal value
c) Post-bronchodilator FEV1/FVC < 70%

Exclusion criteria

For a complete list please see protocol section 5.2.
#. Patients who have had a COPD exacerbation requiring systemic glucocorticosteroid

treatment or antibiotics and/or hospitalization in the 6 weeks prior to screening (Visit 2).
#. Patients requiring oxygen therapy for chronic hypoxemia.
#. Patients who have had a respiratory tract infection within 6 weeks prior to Visit 2.
#. Patients with a history (up to and including Visit 2) of asthma indicated by (but not limited to):
a) onset of respiratory symptoms suggestive of asthma prior to age 40 years
b) history of a diagnosis of asthma
#. Patients with diabetes Type I or uncontrolled diabetes Type II including patients with a history of blood glucose levels consistently outside the normal range or HbA1c > 8.0 % of total hemoglobin measured at Visit 2.
#. Patients with a history (or family history) of long QT syndrome or whose QTc interval (Fridericia) measured at Visit 2 is prolonged.

Study design

Design

Study phase:	3
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):	20-04-2009
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	Indacaterol
Product type:	Medicine

Brand name:	Spiriva
Generic name:	Tiotropium
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-02-2009
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	02-03-2009
Application type:	First submission
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	EUCTR2008-008447-26-NL
CCMO	NL26334.096.09