Randomised, double-blind, placebo-controlled, 6 treatment, 4 period, incomplete cross-over trial to characterise the 24-hour lung function profiles of tiotropium + olodaterol fixed dose combination (2.5/5 µg, 5/5 µg), tiotropium (2.5 µg, 5 µg) and olodaterol (5 µg) (oral inhalation, delivered by the Respimat® Inhaler) after 6 weeks once daily treatment in patients with Chronic Obstructive Pulmonary Disease (COPD)

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The primary objective of the trial is to determine the 24-hour FEV1-time profile of tiotropium + olodaterol FDC (2.5/5 µg, 5/5 µg), administered once daily by the RESPIMAT Inhaler, after 6 weeks of treatment.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON37551

Source
ToetsingOnline

Brief title
VIVACITO

Condition

- Respiratory disorders NEC

Synonym
chronic obstructive pulmonary disease, COPD

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 24 hour lungfunction, COPD, pharmacokinetics, tiotropium/olodaterol

Outcome measures

Primary outcome

FEV1 AUC0-24h response [L] after 6-weeks of treatment.

Secondary outcome

Key secondary endpoints

FEV1 AUC0-12h response [L] after 6-weeks treatment

FEV1 AUC12-24h response [L] after 6-weeks treatment

Secondary endpoints

Trough FEV1 response [L] after 6-weeks treatment

Peak FEV1 responses [L] after 6-weeks treatment

Trough FVC response [L] after 6-weeks treatment

Peak FVC response [L] after 6-weeks treatment

FVC AUC0-24h response [L] after 6-weeks treatment

FVC AUC0-12h response [L] after 6-weeks treatment

FVC AUC12-24h response [L] after 6-weeks treatment

Study description

Background summary

The COPD treatment guidelines advice treatment with bronchodilators with different mechanisms of action. Short acting anticholinergics and beta-2-agonists in fixed dose combinations have shown to be effective and safe and user-friendly for patients. Once daily fixed dose combinations of long-acting anticholinergics for the treatment COPD and will be combined with a once daily long-acting beta-2-agonist, olodaterol. Olodaterol is being developed for the treatment of COPD. It is expected that the combination of these two once daily bonchodilators withdifferent mechanisms of action will provide an optimal long term bronchodilation and is user-friendly for patients.

Study objective

The primary objective of the trial is to determine the 24-hour FEV1-time profile of tiotropium + olodaterol FDC (2.5/5 µg, 5/5 µg), administered once daily by the RESPIMAT Inhaler, after 6 weeks of treatment.

Study design

This is a phase III multi-center, multi-national, randomised, double-blind, placebo-controlled, 6 treatment, 4 period, incomplete cross-over trial.

Intervention

Once daily inhalation of study medication with the Respimat inhaler. Randomization to 4 out of 6 groups (4 treatment periods).

tiotropium + olodaterol 2,5 mcg/5 mcg inhalation solution
tiotropium + olodaterol 5 mcg/5 mcg inhalation solution
tiotropiuim 2,5 mcg inhalation solution
tiotropium 5 mcg inhalation solution
olodaterol 5 mcg inhalation solution
placebo

Restrictions prior to lung function assessments (see E4).

Study burden and risks

At visit 2, 4, 6, and 8, long function tests take place; 30 minutes pre and 30 minutes, 1, 2 and 3 uur post study medication inhalation.
If a site participates in the body box measurements, these tests will be done additionally 1 hour pre inhalation. At visit 2 and 3 bloodsampling series will be done for PK measurements (canula). At visit 2 and 3 urine collection for PK will happen during the day (and at visit 3 also overnight). Visit 2, 4, 6, and 8 last about 7 hours.
At visit 3, 5, 7, and 9 lungfunction tests take place 30 minutes pre and 30 minutes, 1, 2, 3, 4, 6, 8, 10, 12, 22, 23, and 23:50 hours post inhalation.
If a site participates in the body box measurements, these tests will be done additionally 2:30 hour and 24 hour post inhalation.

At these visits the patients will stay overnight in a hotel nearby the hospital (overnight stay, meals and time are compensated).
Patiënts are asked to keep a diary to register inhalation of study- and rescue medication.

Two third of the patients will be randomized to placebo at one of the 4 treatment periods of 6 weeks. This can cause temporary deterioration of their lungfunction. All patients receive Ventolin (supplied by sponsor) for rescue medication, and in all treatment periods patients receive a phone call after three weeks to ask about their health.
Patients on Spiriva, receive Atrovent (supplied by sponsor) for use before randomization and during the 3 week washout periods.

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

1. All patients must sign an informed consent consistent with ICH-GCP guidelines prior to participation in the trial, which includes medication washout and restrictions.
2. All patients must have a diagnosis of chronic obstructive pulmonary disease (P11 05865) and must meet the following spirometric criteria:
Patients must have relatively stable airway obstruction with a post-bronchodilator FEV1 <; 80% of predicted normal and a post-bronchodilator FEV1/FVC < 70% at Visit 1.
3. Male or female patients, 40 years of age or older.
4. Patients must be current or ex-smokers with a smoking history of more than 10 pack years
5. Patients must be able to perform a technically acceptable pulmonary function tests (spirometry), maintain records (patient paper diary) . Applicable for body plethysmography substudy only: perform technically acceptable body plethysmography measurements.
6. Patients must be able to inhale medication in a competent manner from the RESPIMAT Inhaler and from a metered dose inhaler (MDI).

Exclusion criteria

1. Significant diseases other than COPD
2. Patients with a, in the opinion of the investigator, clinically relevant abnormal baseline haematology, blood chemistry, or urinalysis; all patients with an SGOT > x2 ULN, SGPT > x2 ULN, bilirubin > x2 ULN, or creatinine > x2 ULN will be excluded regardless of clinical condition (a repeat laboratory evaluation will not be conducted in these patients).
3. Patients with a history of asthma.
4. Patients with any of the following conditions:
A diagnosis of thyrotoxicosis
A diagnosis of paroxysmal tachycardia
A history of myocardial infarction within 1 year of screening visit (Visit 1).
Unstable or life-threatening cardiac arrhythmia.

Hospitalization for heart failure within the past year.
Known active tuberculosis.
A malignancy for which patient has undergone resection, radiation therapy or chemotherapy within last five years (patients with treated basal cell carcinoma are allowed).
A history of life-threatening pulmonary obstruction
A history of cystic fibrosis.
Clinically evident bronchiectasis.
A history of significant alcohol or drug abuse.
Patients who have undergone thoracotomy with pulmonary resection (patients with a history of thoracotomy for other reasons should be evaluated as per exclusion criterion No. 1).
Patients being treated with oral or patch β-adrenergics.
Patients being treated with oral corticosteroid medication at unstable doses (i.e., less than six weeks on a stable dose) or at doses in excess of the equivalent of 10 mg of prednisone per day or 20 mg every other day.
Patients who regularly use daytime oxygen therapy for more than one hour per day and in the investigator*s opinion will be unable to abstain from the use of oxygen therapy during clinic visits.
Patients who have completed a pulmonary rehabilitation program in the six weeks prior to the screening visit (Visit 1) or patients who are currently in a pulmonary rehabilitation program.
Patients who have taken an investigational drug within one month or six half lives (whichever is greater) prior to screening visit (Visit 1).
Patients with known hypersensitivity to β-adrenergic drugs, BAC, EDTA, or any other component of the RESPIMAT inhalation solution.
Pregnant or nursing women.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-05-2012
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	olodaterol
Product type:	Medicine
Brand name:	Spiriva
Generic name:	tiotropium bromide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-01-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-03-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-04-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	23-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2011-004710-42-NL
CCMO	NL39169.060.11
Other	wordt geregistreerd op clinical trial.gov en clinical trial.us. nr. nog niet beschikbaar