A randomised, double-blind, placebo- and active-controlled parallel group study to assess the efficacy of 12 weeks of once daily treatment of two doses of orally inhaled tiotropium + olodaterol fixed dose combination (delivered by the Respimat inhaler) in patients with Chronic Obstructive Pulmonary Disease (COPD)

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The objective of the proposed study (1237.25) is to evaluate maximal treatment effect in FEV1 and SGRQ after 12-weeks treatment with two different doses of tiotropium + olodaterol FDC (5*g/ 5*g and 5*g/ 2.5*g) by comparison with placebo in patients...

Ethical review	Not approved
Status	Will not start
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON38556

Source
ToetsingOnline

Brief title
OTEMTO 1

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: COPD, Efficacy, Placebo-controlled, Tiotropium-olodaterol

Outcome measures

Primary outcome

There are three primary study parameters/ outcome in this study which are

analysed after 12 weeks of treatment:

* FEV1 AUC0-3h response

* Trough FEV1 response, and

* SGRQ (total score). This endpoint will be evaluated in this trial as well as

after combining the data from this and the replicate trial 1237.26.

Secondary outcome

The secundary study parameters/ outcome in this study which are analysed after

12 weeks of treatment are:

* FVC (forced vital capacity) AUC0-3h response (L)

* Trough FVC response (L)

* FEV1 peak 0-3h response

* FVC peak 0-3h response

* FEV1 response (L) at 5,15 and 30 minutes, and at 1,2 and 3 hours after

inhalation of study medication, and

* FVC response (L) at 5,15 and 30 minutes, and at 1,2 and 3 hours after

inhalation of study medication.

Study description

Background summary

The COPD treatment guidelines advise treatment with bronchodilators with different mechanisms of action. Short-acting anticholinergics and beta2-agonists in fixed dose combinations have shown to be effective and safe and are user-friendly to patients. Once daily fixed dose combinations of long-acting anticholinergics and beta2-agonists are not yet available. Tiotropium bromide is a registered once daily long-acting anticholinergic for the treatment of COPD and will be combined with a once daily long-acting beta2-agonist, olodaterol, in this study. Olodaterol is being developed for the treatment of COPD. It is expected that the combination of these two once daily bronchodilators with different mechanisms of action will provide an optimal long term bronchdilation and is user-friendly.

Earlier studies established a satisfactory safety and tolerability profile of 4 weeks once daily treatment with tiotropium + olodaterol and also provided evidence of the additional bronchodilator efficacy of tiotropium + olodaterol FDC compared with tiotropium monotherapy or olodaterol monotherapy. Based on the evidence of the efficacy and safety of the fixed dose combination of tiotropium and olodaterol up to 4 weeks treatment in patients with COPD, it is considered appropriate to progress into the next phase of clinical development and conduct long-term, confirmatory trials to provide substantial evidence of the efficacy and safety of tiotropium + olodaterol FDC in patients with COPD.

Currently two identical studies are running with a treatment phase of 1 year. However, in these studies a placebo arm is missing. The present study 1237.25 and its replicate 1237.26 have been designed to allow for the inclusion of a placebo control arm by restricting the treatment duration to 12 weeks and restricting the study population to patients with moderate to severe COPD. The comparison with placebo is intended to provide further evidence of the maximal clinical efficacy of tiotropium + olodaterol FDC. The active control arm (5 *g tiotropium) has been included to allow for cross-trial comparisons (i.e.

comparison of the relative efficacy of tiotropium + olodaterol FDC vs. tiotropium observed in
studies 1237.25/1237.26 with the relative efficacy of tiotropium + olodaterol FDC vs. tiotropium observed in the other 1 yr studies.

Study objective

The objective of the proposed study (1237.25) is to evaluate maximal treatment effect in FEV1 and SGRQ after 12-weeks treatment with two different doses of tiotropium + olodaterol FDC (5*g/ 5*g and 5*g/ 2.5*g) by comparison with placebo in patients with COPD.

Study design

After signing informed consent and completing an initial screening visit (Visit 1), patients will enter a 2 week run-in period to ensure clinical stability (i.e. no exacerbations).
Patients who meet all the inclusion criteria and none of the exclusion criteria will be randomized at Visit 2 into one of the following treatmentarms:
1) tiotropium + olodaterol (5 / 5 *g) fixed dose combination inhalation solution, delivered once daily via the RESPIMAT
2) tiotropium + olodaterol (2.5 / 5 *g) fixed dose combination inhalation solution, delivered once daily via the RESPIMAT
3) tiotropium (5 *g) inhalation solution, delivered once daily via the RESPIMAT, and
4) placebo inhalation solution, delivered once daily via the RESPIMAT.
The treatment will take 12 weeks. Patients will be evaluated for an additional 21 days following completion of the treatment period, or, in case of early discontinuation, after the final dose of study medication. During these 3 weeks the patient may return to his/her usual medication as used before the study.
An interactive voice response system (IVRS) will be used for randomization to a treatment arm. It is a double-blind, placebo and actively controlled randomised study with parallel groups.

Intervention

During twelve weeks a once daily inhalation of studymedication with the Respimat® inhaler with one of the following treatment arms (randomisation 1:1:1:1) - fixed dose combinatie tiotropium-olodaterol 2.5 *g / 5 *g - fixed dose combinatie tiotropium-olodaterol 5 *g / 5 *g - tiotropium 5 *g , and - placebo. During five visits spirometry will be performed. , body plethysmography during Visit 1 and in total 7 cycle ergometry tests will be done.

Study burden and risks

During the course of the study each patient performs 5 times spirometry. In principle, no serious risks are involved in spirometry. Nevertheless, risks and discomforts associated with lung function testing may include shortness of breath, dizziness, or headache during the breathing tests. Should this occur, the patient may receive treatment. During the study two times (or if necessary three times) a physical examination is performed. During three visits the patient will be asked to complete questionnaires. In addition the patient Apart from that ijgt de patient aan het begin van het onderzoek een (electronisch) dagboekje mee om iedere dag de PEF waarde te meten. PEF is de maximale volumestroom bij geforceerde uitademing, vanuit volledige inspiratie, uitgedrukt in liters per minuut. Ook wordt het gebruik van rescue medicatie geregistreerd in het dagboekje.

During the screeningperiod some medication will be washed-out. For this reason, all patients will receive Ventolin as rescue medication already at start of screeningperiod and may also be used during the treatmentperiod. Besides that, Atrovent may be used during screeningperiod. Oral and inhaled corticosteroids are also accepted throughout the study. There are also some restrictions for a patient in terms of food and fluid intake as well as in physical activities performed in the period before each visit. Inhalation of studymedication may cause side effects. Normally, these side effects are mild and they usually disappear with continued treatment. Safety monitoring will include bloodsampling, measurement of vital signs and ECG monitoring. Bloodsampling may also cause some inconvenience.
The total time spent for each patient is 14-19.5 hours.

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

- Diagnosis chronic obstructive pulmonary disease
- Relatively stable airway obstruction with post FEV1 ><=30 and
< 80% predicted normal and post FEV1/ FVC < 70%
- Male or female patients, 40 years of age or more
- Smoking history more than 10 pack years

Exclusion criteria

- Significant diseases other than COPD
- History of asthma
- COPD exacerbation in previous 3 months
- Completion of pulmonary rehabilitation program within previous 6 weeks or current participation in pulmonary rehabilitation program.
- Pregnant or nursing women
- Patients unable to comply with pulmonary medication restrictions

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:	Will not start
Enrollment:	62
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	Tiotropium-olodaterol FDC (fixed dose combination)
Product type:	Medicine
Brand name:	Spiriva
Generic name:	Tiotropium bromide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	25-09-2013
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Not approved

Date:	28-10-2013
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	EUCTR2013-002243-29-NL
CCMO	NL45379.096.13
Other	nog niet bekend