A randomized, double-blind, placebo controlled, multicentre study to determine the effect of QVA149 on lungfunction in patients with Chronic Obstructive Pulmonary Disease (COPD).

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON32011

Source
ToetsingOnline

Brief title
QVA2204

Condition

- Respiratory tract infections

Synonym
COPD, lungemphysema

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: de industrie zoals opgegeven bij B6.

Intervention

Keyword: COPD, Cross over design, Placebo, QVA149

Outcome measures

Primary outcome

To demonstrate the superior bronchodilatory efficacy of QVA149 300/50 versus placebo in patients with moderate to severe stable COPD in terms of trough FEV1 (mean of evaluations at 23h 15min and 23h 45min post dose) following 7 days of treatment delivered by the Concept1 Single Dose Dry Powder Inhaler (SDDPI).

Secondary outcome

The key secondary comparison will compare the bronchodilatory efficacy of QVA149 300/50 versus QAB149 300µg in terms of trough FEV1 following 7 days of treatment.

Additional secondary comparisons:

* To compare the bronchodilatory efficacy of QVA149 300/50 versus QAB149 600µg in terms of trough FEV1 following 7 days of treatment.

* To compare the bronchodilatory efficacy of QVA149 300/50 versus QAB149 300µg and QAB149 600µg in terms of FEV1 AUC5min-12h following 7 days of treatment.

* To assess the safety and tolerability of QVA149 300/50 and QAB149 (300µg and

600µg)

delivered by the Single Dose Dry Powder Inhaler (SDDPI) in terms of

post-inhalation events, ECGs, laboratory tests, blood pressure and adverse

events.

Study description

Background summary

Currently, there is no fixed-dose combination of a long-acting ß2-agonist and a long-acting muscarinic antagonist. Combivent® (albuterol (salbutamol) sulfate and ipratropium bromide) is a short-acting fixed dose combination of a ß2-agonist and a muscarinic antagonist indicated for the treatment of COPD and administered with two inhalations four times daily. Published studies have shown that the complementary mechanisms of action of a long-acting ß2-agonist (formoterol) and a long-acting muscarinic antagonist (tiotropium bromide) significantly improve bronchodilation in COPD patients compared to the respective monotherapies.

Study objective

The purpose of this study is to evaluate the effects of QVA149 300/50, a fixed dose combination of QAB149 300µg and NVA237 50µg, versus placebo and two doses of QAB149 300µg and 600µg, in terms of lung function in patients with moderate to severe stable COPD before proceeding to phase III development.

Study design

This is a randomized, double-blind, 4 period cross-over, multi-centre study to evaluate the efficacy and safety of QVA149 300/50 versus placebo and two doses of QAB149 in patients with moderate to severe stable COPD. Patients entered into this study will be 40 years old or older with a diagnosis of moderate to severe COPD and will have experienced no COPD exacerbations in the 6 weeks preceding visit 1.

Screening visit 1
An initial screening visit (Visit 1) will be used to assess suitability for the study, to obtain relevant background information and to obtain informed consent (informed consent may be obtained by the investigator prior to Visit 1 to allow patients sufficient time to consider participation in this study). Patients who are currently using a prohibited medication will enter a washout period of up

to 7 days before returning for the second screening visit (Visit 2). Screening visit 2 Patients not using any prohibited medication will proceed directly to the second screening visit (i.e. Visits 1 and 2 may be combined for patients not taking prohibited medication). At this screening visit patients will undergo further tests including screening spirometry and a ß2agonist bronchodilator reversibility test. Patients who meet the inclusion / exclusion criteria at this screening visit will return to the study centre on the next day, or as soon as possible afterwards for the baseline / randomization visit (Visit 3).

Study Treatment Periods
At the baseline visit (Visit 3), patients whose eligibility is confirmed will be randomized to one of the available treatment sequences in this four period cross-over design. Patients will then enter the first of four double-blind, 7 day treatment periods. Patients will be assessed on consecutive days at the beginning and end of each treatment period (the first and second days and the seventh and eighth days). The assessment to address the primary objective (trough FEV1) will be performed on the eighth day of each treatment period. On the first day of each treatment period patients will be required to remain at the study centre until 4 hours after taking study medication. Patients will then return on the next day to complete the 23h 15min and 23h 45min post dose spirometry. On the seventh day of the treatment period patients will be required to remain at the study centre until 12 hours after taking study medication and will return on the next day (eighth day) to complete the 23h 15min and 23h 45min post dose spirometry. In total patients will be required to attend the study centre for 18 visits. In a subgroup of patients pharmacokinetic sampling will be performed on the seventh and eighth days of each of the four treatment periods.
Patients will complete all four study periods according to the randomization sequence with a 7 day wash out between study periods during which the use of a fixed dose combination of a short acting ß2 agonist and short acting muscarinic antagonist as indicated is permitted if considered necessary by the investigator (this combination may also be used during the screening period if deemed necessary by the investigator). The last dose should not be taken later than 8h before the next study visit.
During the study patients will be permitted to use allowable COPD medications described in section 5.1, and will be provided with a salbutamol/albuterol inhaler to use as rescue medication during the four 7 day treatment periods. Patients will be asked to abstain wherever possible from using rescue medication during study visits, and in the six hours prior to attending a study visit.

Intervention

QVA149 300/50mcg
QAB149 600mcg
QAB149 300mcg

placebo

salbutamol as rescue medication
inhalatiecorticosteroïd
Combivent or Berodual during the wash-out periods

Study burden and risks

It cannot be guaranteed that the health of each individual patient will improve by participating in this study. Patients will be checked up regularly during this study and medication will be provided at no costs. The results of this study might help other patients with COPD.
Possible discomforts of the study are:
Physical Examination 6 times, reversibility test once, spirometry during 17 visits (12 hours postdose and 4 hours postdose at certain visits), blood collection at 10 visits, urine collection at 9 visits, EGCs will be taken during 17 visits and 3 pregnancy tests will be taken, if applicable.

Contacts

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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

- Male or female patients aged 40 years and older
- Patients with moderate to severe stable COPD according to GOLD Guidelines 2006
- Patients who have a smoking history of at least 10 pack years
- Patients with a post-bronchodilator FEV1 equal or greater than 30% of the predicted normal value and less than 80% of the predicted normal value, and post bronchodilator FEV1/FVC less than 0.7.

Exclusion criteria

- Patients requiring long term oxygen therapy;
- Patients who have had a respiratory tract infection within 6 weeks prior to visit 1;
- Patients with any history of asthma indicated by (but not limited to) a blood eosinophil count > 400mm3;
- Patients with uncontrolled type 1 and type 2 diabetes including patients with a history of blood glucose levels consistently outside the normal range, or HbA1c > 8% of total Hb measured at visit 1;
- Patients with a history of long QT syndrome or whose QTc interval measured at visit 2 is prolonged.

Study design

Design

Study phase:	2
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):	07-04-2008
Enrollment:	36
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-11-2007
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	23-01-2008
Application type:	First submission
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	EUCTR2007-003655-36-NL
CCMO	NL20419.003.07