A study to compare the efficacy and safety of once daily QVA149 vs. the once daily concurrent administration of QAB149 plus NVA237 in patients with moderate to severe chronic obstructive pulmonary disease (CQVA149A2326)

Published: 05-03-2012
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Primary objective: To evaluate the non-inferiority of QVA149 110/50 µg qd as compared to concurrentadministration of QAB149 150 µg qd plus NVA237 50 µg qd in terms of its effect on trough FEV1 (mean of 23 h 15 min and 23 h 45 min post-dose)...

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

Summary

ID

NL-OMON37459

Source
ToetsingOnline

Brief title
CQVA149A2326

Condition

- Respiratory disorders NEC

Synonym
COPD; chronic obstructive pulmonary disease

Research involving

Human

Sponsors and support

Primary sponsor: Novartis Pharma BV
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: COPD, indacaterol, NVA237, QVA149

Outcome measures

Primary outcome

Trough FEV1 week 4.

Secondary outcome

FEV1, rescue medication, COPD symptoms, safety and tolerability.

Study description

Background summary

In patients with COPD, exacerbations of their condition are a common cause of ill health, hospitalization and deaths. Frequent COPD exacerbations are associated with impairment in quality of life and increased rate of decline in lung function. Treatment of COPD exacerbation accounts for a great burden on the health care system. Therefore effective management of COPD includes both prevention and treatment of COPD exacerbation. Current data indicates that long-acting beta agonists (LABAs) combined with corticosteroids or long-acting muscarinic antagonists (LAMAs, e.g. Spiriva®) reduces the rate of COPD exacerbations. Both LABAs and LAMAs as monotherapy are effective in providing long-term bronchodilation in terms of improvement in FEV1 but the possible beneficial effects of LABAs and LAMAs as fixed-dose combination on COPD exacerbations has to be
demonstrated.
QVA149 is a fixed dose combination of a LABA (indacaterol - QAB149) and a LAMA (glycopyrronium bromide - NVA237). The selection of QVA149 dose in this study (110/50 µg once daily) was based on data from the QAB149 and NVA237 monotherapy programmes. Those programmes identified 150 µg once daily for QAB149, and 50 µg once daily for NVA237. However, in formulating the QVA149 combination product, an increase in fine particle (respirable) fraction was observed for the QAB149

component (compared with the monotherapy). As a consequence, to ensure that the fine particle dose of QAB149 delivered to the lung from the combination matches that delivered from the monotherapy, the dose for the QAB149 component of QVA149 has been reduced to 110 µg.
The current phase III study is part of the COPD development programme. In this study the effects of QVA149 are being compared with those of the individual components. This non-inferiority study is mandatory for the registration dossier of a combination product. It is expected that the combination product QVA149 will provide more convenience to the patient and will (tus) enhance compliance, and that the efficicay will be similar to that of a combination of both individual products.

Study objective

Primary objective: To evaluate the non-inferiority of QVA149 110/50 µg qd as compared to concurrent
administration of QAB149 150 µg qd plus NVA237 50 µg qd in terms of its effect on trough FEV1 (mean of 23 h 15 min and 23 h 45 min post-dose) following 28 days of blinded treatment in patients with moderate to severe chronic obstructive pulmonary disease.
Secondary objectives: FEV1, rescue medication, COPD symptoms, safety and tolerability.

Study design

Randomized double blind, parallel group phase III study. Screening, s.n. adjustment current COPD medication, followed by 2 week run-in period (indacaterol 150 mcg en NVA237 50 mcg dd). Thereafter randomisation (1:1) to treatment of 4 weeks with:
• QVA149 110/50 mcg o.d.
• Indacaterol 150 mcg o.d. and NVA237 50 mcg o.d.
via dry powder inhaler.
Salbutamol rescue medication.
Total study duration approx. 6-7 weeks.
Approx. 184 patients.

Intervention

Treatment with QVA149 or indacaterol plus NVA237.

Study burden and risks

Risk: Adverse effects of study medication. Changes in current COPD medication.
Belasting: 6 visits and 3 phone calls in 6-7 weeks.
Daily electronic diary (signs, symptoms, rescue medication). Physical exam 3x, blood tests (safety) 3x (approx. 10 ml blood/visit, total amount 30 ml),

pregnancy test 3x, 1x pulmonary function test with reversibility, 2x 8 pulmonary function tests in 5 hours plus 2 tests next morning, 3x ECG.

Contacts

Public
Novartis Pharma BV

Raapopseweg 1
6824 DP Arnhme
NL
Scientific
Novartis Pharma BV

Raapopseweg 1
6824 DP Arnhme
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female adults aged >=40 years.
• Patients with moderate to severe COPD (Stage II-III) according to the (GOLD Guidelines, 2010).
• Current or ex-smokers who have a smoking history of at least 10 pack years.
• Post-bronchodilator FEV1 >=30% of the predicted normal value, and postbronchodilator FEV1/FVC < 0.70.
• COPD symptoms during run-in phase.

Exclusion criteria

• Diabetes type I and uncontrolled diabetes type 2.
• History of long QT syndrome or QTc measured at Visit 2 (Fridericia method) is prolonged (>450 ms for males and females).
• BMI >=40 kg/m2.
• Patients who have had a COPD exacerbation in the 6 weeks prior to Visit 1.
• Patients who have had a respiratory tract infection within 4 weeks prior to Visit 1.
• Pregnancy and breast feeding. Inadequate contraception, if relevant.

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):	15-05-2012
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	glycopyrronium bromide
Generic name:	glycopyrronium bromide
Product type:	Medicine
Brand name:	Onbrez

Generic name:	indacaterol
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	QVA149
Generic name:	QVA149

Ethics review

Approved WMO Date:	05-03-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-04-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-06-2012
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-07-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-12-2012
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
Other	clinicaltrials.gov registratienummer n.n.b.
EudraCT	EUCTR2011-006050-91-NL
CCMO	NL40008.060.12