A randomized, double-blind, placebo-controlled, 2-period, cross-over study to assess the efficacy and safety of differing doses of NVA237 administered either once daily or twice daily, in patients with moderate to severe chronic obstructive pulmonary disease (COPD)

Published: 01-04-2010
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Primary objectiveTo evaluate the relationship of incremental doses of NVA237 q.d. and b.i.d. and their effect on trough FEV1 after 28 days of treatment, as defined by the percentage of the maximal effect that each dose achieves in relation to the...

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

Summary

ID

NL-OMON34643

Source
ToetsingOnline

Brief title
CNVA237A2208

Condition

- Respiratory disorders NEC

Synonym
chronic obstructive pulmonary disease, COPD

Research involving
Human

Sponsors and support

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

Intervention

Keyword: COPD, dose finding, NVA237

Outcome measures

Primary outcome

Relationship of incremental doses of NVA237 q.d. and b.i.d. and their effect on

trough FEV1 after 28 days of treatment, as defined by the percentage of the

maximal effect that each dose achieves in relation to the maximal effect of

NVA237. (Trough is defined as the mean of FEV1

measurements at 23 h 15 min and 23 h 45 min post morning dose).

Secondary outcome

Use of rescue medication, FEV1 (AUC 0-24 h and shorter intervals, peak and 12

h), FVC, safety.

Study description

Background summary

NVA237 is a synthetic quaternary ammonium compound that acts as a competitive antagonist at muscarinic
acetylcholine receptors and is being developed as a once-daily inhalation treatment to be delivered by the Novartis
Single Dose Dry Powder Inhaler (SDDPI) for patients with COPD. Inhaled anticholinergic drugs such as ipratrompium
bromide (Atrovent®) and Tiotropium bromide (Spiriva®) have been approved in the US and European Union for the

treatment of COPD.
This study is designed to support the registration of NVA237 worldwide, including the US and the EU.

Study objective

Primary objective
To evaluate the relationship of incremental doses of NVA237 q.d. and b.i.d. and their effect on trough FEV1 after 28 days of treatment, as defined by the percentage of the maximal effect that each dose achieves in relation to the maximal effect of NVA237. (Trough is defined as the mean of FEV1 measurements at 23 h 15 min and 23 h 45 min post morning dose).
Key secondary objective
To evaluate the magnitude of any difference of effect on trough FEV1 after 28 days of treatment between the same total daily doses of NVA237 by comparing once daily and twice daily dosing regimens.

Study design

Randomized, double blind, placebo controlled cross over phase II study . 8 treatments, balanced incomplete block design. qd or bid dosing. Pre-screening, s.n. adjustment current COPD treatment, followed by 2nd screening and 1 week run-in period. Thereafter randomization to 16 independent treatment sequences. All patients will be given 2 treatments, separated by a washout period of 1 week.
Treatments:
1. Qd NVA237 12,5 mcg
2. Qd NVA237 25 mcg
3. Qd NVA237 50 mcg
4. Qd daags NVA237 100 mcg
5. Bid NVA237 12,5 mcg
6. BidNVA237 25 mcg
7. Bid NVA237 50 mcg
8. Placebo.
via single dose powder inhaler.
Salbutamol rescue medication.
Total study duration approx. 11 weeks.
Approx. 360 randomized patients (>500 screened).

Intervention

NVA237 or placebo.

Study burden and risks

Risks: Adverse events of study medication. Changes in current COPD medication.

Burden: 11-12 visits in 11 weeks, thereoff 6 days of 24 h measurements (incl. hotel overnight stay) and 2 days of 9h measurements. Daily diary. Safety blood 3x.Approx. 10 ml blood per visit, total volume ca. 30 ml. Pregnancy test 2x. Normal visits: 3x. Vital signs (plus or minus physical exam) 1 visit. Pulmonary function tests 2x per visit (1 visit with reversibility). EKG 1 visit.
9h visits: 2x. Duration 9h. 6x pulmonary function tests. 1x vital signs.
24h visits: 6x. Duration 24h. 6x overnight stay in hotel with nightly measurements. 14-17 pulm. function tests. 0-1 EKG and 1-3x vital signs per visit.

Contacts

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Novartis

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Scientific
Novartis

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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 or female adults aged 40 years and above.

2. Moderate to severe stable COPD (Stage II or Stage III) according to the (GOLD Guidelines 2008).
3. Smoking history of at least 10 pack years.
4. Post-bronchodilator FEV1 >30% and < 80% of the predicted normal.
5. FEV1/FVC ratio <70% (post bronchodilation).

Exclusion criteria

• Lower airway infection in the past 4 weeks.
• Bronchial asthma.
• Type I and uncontrolled type II diabetes.
• α1-antitrypsin deficiency.
• Other relevant pulmonary diseases.
• Contra-indications for anticholinergics.
• Use of ceratin COPD and other medications (see protocol for details).
• Vaccination with live or inactivated vaccines in the past 30 and 2 days resp.
• Longterm oxygen therapy.
• Pregnancy and breast feeding. Inadequate contraception, if relevant.

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):	09-06-2010
Enrollment:	58
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NVA237
Generic name:	NVA237

Ethics review

Approved WMO Date:	01-04-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-04-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-05-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-09-2010
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 nog niet bekend
EudraCT	EUCTR2009-014038-11-NL
CCMO	NL31828.060.10