A 26-week treatment, randomized, double-blind, placebo-controlled, parallel group study to assess the efficacy, safety and tolerability of NVA237 in patients with chronic obstructive pulmonary disease (CNVA237A2304)

Published: 28-12-2009
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Primary objectivesTo confirm that NVA237 50µg o.d. (delivered via a SDDPI) vs. placebo significantly increases trough FEV1 (defined as mean evaluation at 23 h 15 min and 23 h 45 min post dose) following 12 weeks of treatment in patients with...

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

Summary

ID

NL-OMON34669

Source
ToetsingOnline

Brief title
CNVA237A2304

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, NVA237, Placebo

Outcome measures

Primary outcome

Pulmonary function parameters at trough.

Secondary outcome

Transition Dyspnea Index (TDI), St George*s Respiratory Questionnaire (SGRQ),time to 1st exacerbation, number of exacerbations, use of rescue medication, all measurements of pulmonary function parameters , signs and symptoms, adverse events.

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 provide pivotal confirmation of efficacy and long term safety data for the 50µg o.d. dose of NVA237 in patients with moderate to severe chronic obstructive pulmonary disease (GOLD Guidelines, 2008). Data obtained from this study is intended to be used to support the registration of NVA237 worldwide, including the US and the EU.

Study objective

Primary objectives
To confirm that NVA237 50µg o.d. (delivered via a SDDPI) vs. placebo significantly increases trough FEV1 (defined as mean evaluation at 23 h 15 min and 23 h 45 min post dose) following 12 weeks of treatment in patients with moderate to severe COPD (GOLD Guidelines 2008)
Secondary objectives
Key
• To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on breathlessness measured using the Transition Dyspnea Index (TDI) after 26 weeks treatment.
• To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on the health status by measuring the total score of the St George*s Respiratory Questionnaire (SGRQ) after 26 weeks treatment.
Important secondary objectives/variables
To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on time to first COPD exacerbation during 26 weeks treatment.
To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on daily rescue medication use (number of puffs) over 26 weeks.
Additional Secondary Comparisons
To evaluate the effect of NVA237 (50µg o.d.) on lung function (FEV1, FVC) at all timepoints (including FEV1AUC5min-12h and FEV1AUC5min-24h in a subset of 250 patients; approximately 167 NVA237: 83 placebo), as compared with placebo, with respect to the early response, approximate peak response and trough response.
• To assess the potential effect of NVA237 (50µg o.d.) on cardiovascular safety using 24 hour Holter monitoring data in a subset of 80 patients.
• To assess safety and tolerability of NVA237 (50µg o.d.) with regard to vital signs, ECGs, laboratory evaluations and adverse events over 26 weeks.
• To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on rate of COPD exacerbations during the 26 week randomized treatment period.
• To evaluate the effect of NVA237 (50µg o.d.) vs. placebo on other COPD symptoms collected via patient diary over the 26 week randomized treatment period.

Study design

The study is a 26 week randomized multi-center, double-blind, placebo-controlled parallel group design. All study treatments are given in addition to permitted COPD background therapy as outlined in Section 6.5.7. At an initial pre-screening visit (Visit 1) informed consent will be obtained, current COPD medications reviewed and if necessary arrangements made to adjust prohibited COPD therapy to allowable COPD therapy. At Visit 2 (up to 7 days after initial visit) screening assessments will be performed including spirometry and reversibility testing. Between Visit 2 and Visit 3 there is a 14 day run-in period used to assess eligibility of patients for the study and to collect baseline patient diary data. At Visit 3 patients meeting the inclusion/exclusion criteria will be randomized to receive double-blind NVA237 50µg o.d. or placebo in a ratio of 2:1, for a 26 week treatment period.

After patients receive their first dose on day 1 (Visit 3) they will remain at the study site to complete spirometric and safety assessments for up to 4 hours (up to 12 hours for a subset of patients included in the 24 h serial spirometry group). Patients will return to the center the following day for spirometric assessments.
Patients will be required to attend the study center for 10 more visits (total 13). After 12 weeks (assessment of the primary efficacy variable, trough FEV1) and 26 weeks there are visits on consecutive days to ensure *trough* spirometry data are accurately collected.
12 hour serial spirometry will be conducted in the clinic, in a subset of patients (approximately 250 randomized patients) at designated centers, at day 1 (Visit 3). The same subset of patients will perform 24 hour serial spirometry at week 12 (Visit 8) and at week 26 (Visit 12). All patients will perform spirometry up to 4 hours post dose at day 1 (Visit 3), week 12 (Visit 8) and week 26 (Visit 12).
SGRQ and BDI/TDI will be assessed in all patients at day 1 (Visit 3), week 12 (Visit 8) and week 26 (Visit 12).
24 h Holter monitoring will be conducted in a subset of patients (approximately 80 randomized patients) at Visit 2, 3, 8 and 12. Note: baseline Holter monitoring will begin the day before Visit 2.
PK sampling will be conducted in a subset of patients (approximately 240 randomized patients) at Visit 3, 4, 5, 8, 9, 12 and 13.
During the study patients will be permitted to use allowable COPD medications described in Section 6.5.7 and will be provided with a salbutamol/albuterol inhaler to use as rescue medication. 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.
If a patient experiences a COPD exacerbation during the treatment period he/she will be treated as deemed appropriate by the Investigator for the exacerbation, a standardized treatment plan (see section 7.4.4) is provided for reference. Following treatment for the exacerbation the patient will be expected to continue in the study if, in the opinion of the investigator, he/she can be safely returned to their pre-exacerbation concomitant medications. If following the exacerbation, the patient requires the addition of new concomitant COPD medications, then he/she should be withdrawn from the study. At the end of an exacerbation the patient must attend the clinic for assessment of the episode.

Intervention

Patients will be randomized to treatment with NVA237 50µg o.d., or placebo to NVA237 in a ratio of 2:1.

Study burden and risks

Adverse events of study medication. Changes in current COPD medication.
13 visits in 29 weeks, 3 days of extended measurements. Daily diary. Safety

blood 6x. Ca. 10 ml blood per visit, total volume ca. 60 ml. Pregnancy test 4x.
Normal visits: 10x. Vital signs (plus or minus physical exam) all visits.
Pulmonary function tests 1-6x per visit (1x with reversibility). EKG 2 visits.
Extended visits: 3x. Duration 14-24 h. 2x overnight stay in hospital with nightly measurements. 13-15 pulm. function tests. 3 EKGs en 4x vital signs per visit.
Optional: PK blood sampling during 7 visits. 1-7 samples of 3 ml per visit.
Total 27 samples, ca. 80 ml.
NB: Holter monitoring and PG blood sampling NOT IN NL.

Contacts

Public
Novartis

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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

1. Male or female adults aged >=40 years, who have signed an Informed Consent Form prior

to initiation of any study-related procedure.
2. Patients with moderate to severe stable COPD (Stage II or Stage III) according to the (GOLD Guidelines 2008).
3. Current or ex-smokers who have a smoking history of at least 10 pack years. (Ten pack-years are defined as 20 cigarettes a day for 10 years, or 10 cigarettes a day for 20 years etc.)
4. Patients with a post-bronchodilator FEV1 >=30% and < 80% of the predicted normal, and post-bronchodilator FEV1/FVC < 0.7 at Visit 2 (day -14)
5. Patients, according to daily electronic diary data between Visit 2 (-14) and Visit 3 (day 1), with a total score of 1 or more on at least 4 of the last 7 days prior to Visit 3

Exclusion criteria

• Oxygen therapy.
• Lower airway infection in the past 6 weeks.
• Bronchial asthma.
• α1-antitrypsin deficiency.
• Other relevant pulmonary diseases.
• Use of ceratin COPD medications (see protocol for details).
• 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:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-03-2010
Enrollment:	32

Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	28-12-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-01-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-03-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-04-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2010
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-08-2010
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	EUCTR2009-013504-32-NL
CCMO	NL30677.060.09