A two part, double blind, placebo controlled, study to assess the safety, tolerability, pharmacokinetics and pharmacodynamic effects of multiple doses of QBM076 in patients with COPD

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Primary Obejective:To evaluate the preliminary efficacy of 8 consecutive weeks of QBM076 in current or ex-smoking patients with stable COPD with spirometry grades I-III (according to the current GOLD strategy (GOLD 2013).Secondary Objectives:To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON41772

Source
ToetsingOnline

Brief title
QBM076X2203

Condition

- Bronchial disorders (excl neoplasms)

Synonym
chronic lung disease, smokers cough

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V.;de sponsor/verrichter van dit onderzoek.

Intervention

Keyword: COPD, pharmacokinetics, QBM076, safety

Outcome measures

Primary outcome

- LCI

- Absolute number of sputum neutrophils

- FEV1

- TDI.

Secondary outcome

- Respiratory resistance

- All vital signs data

- All ECG data

- All laboratory data

- All information obtained on adverse events

- An exploratory analysis of the relationship between pharmacokinetic and

pharmacodynamic measures.

Study description

Background summary

COPD is a progressive condition that is a major cause of poor health and death worldwide and contributes significantly to health care costs and comorbidity.

COPD is a highly heterogeneous disease that is characterized by poorly reversible airflow limitation that is progressive, and associated with abnormal inflammatory response of the lung. By suppressing neutrophil influx it is postulated that reduced inflammation and/or increased repair will take place.

QBM076 choline salt is an orally administered low molecular weight CXCR2 antagonist specifically developed for the treatment of COPD. Inhibition of CXCR2 receptor in vivo with QBM076 will block neutrophil migration. By reducing CXCR2 activation, it is postulated inflammation within the lung will be reduced resulting in improved function of the small airways and a slowdown of tissue.

Recently, COPD has been determined to be a progressive and potentially reversible disease beginning and manifesting pathology throughout the disease process in the small airways. As the disease progresses, the large airways become involved. Current standards of treatment efficacy focus on PFTs, and in particular, FEV1, which is a measure primarily of the larger conducting airways. This study focuses on COPD patients with measurable small airway disease, physiologically and phenotypically, to preselect patients who may have the greatest benefit from QBM076, a selective CXCR2 inhibitor.

The improvement of the ventilation and perfusion of smaller airways of the lung with concomitant improvement in their function, will result in either prevention of further deterioration or clinical improvement in longer studies manifested by fewer exacerbations. Thus there may be an improvement in both the quality and quantity COPD patients* lives through a novel mechanism of action.

Study objective

Primary Obejective:
To evaluate the preliminary efficacy of 8 consecutive weeks of QBM076 in current or ex-smoking patients with stable COPD with spirometry grades I-III (according to the current GOLD strategy (GOLD 2013).

Secondary Objectives:
To assess the safety and tolerability of multiple doses of QBM076 in current or ex-smoking COPD patients for 8 consecutive weeks
* To evaluate the pharmacokinetics of multiple doses of QBM076 for 8 consecutive weeks
* To evaluate the preliminary efficacy after 8 consecutive weeks of multiple doses of QBM076 in COPD patients as reflected in changes in:
- Measurements associated with MBNW such as Scond and Sacin, trapped gas volume, closing volume
- Change in % sputum neutrophils in sputum
- FEF25-75, FEV3/FVC, 1-(FEV3/FVC), FEV6, FEV1/FEV6 and post-bronchodilator FEV1 measured by spirometry
- Additional PFT measurements performed in a body plethysmography box including DLCO, IC, FRC, TLC, RV and RV/TLC ratio

- Assessment of the change from baseline in quantitative air trapping as assessed by HRCT

Study design

This is a two part, double-blind placebo-controlled study of the safety, tolerability, pharmacokinetic and pharmacodynamic effects of multiple doses QBM076 in patients with COPD. Part 1 has been completed in which the Netherlands has not participated. Netherlands participates in Part 2.
Part 2 of this study begins with a screening of a maximum of 30 days, followed by a treatment period (QBM076 / placebo) of 8 weeks. Approximately one week after the treatment period, there is a final end of study visit (control). For each subject the total duration of the study is approximately 14 weeks and approximately 12 visits will be performed.

Intervention

Treatment with QBM076 150 mg / placebo (oral): daily, for 8 weeks.

Study burden and risks

Disadvantages of participating is the risk of side effects from the study medication and discomfort of the test procedures.

Possible side effects of QBM076:
Headache (most often reported) and increase sensitivity to sunlight / UV light.

Inconvenience/Risk of the studyprocedures:
- Blood prick; local pain, bruising, scab infection.

- During the blowing of a lung; headache, chest pressure or light-headedness. After inhalation of salbutamol: tremors or palpitations.
- When coughing up sputum: chest tightness, wheezing, light-headedness or an unpleasant taste in the mouth.
- When a CT scan is radiation-free, however very gering.Tijdens staying in the scanner; suffer from anxiety in a small space (claustrophobia).

Burden:
- Physical examination: 6x
- Blood pressure and pulse: 12x
- Temperature, oxygen content: 12x
- Blood collection/tests: 12x
- Pregnancy test (female subjects): 6x
- Urinalysis: 7x
- ECG: 9x
- PFT spirometry: 8x
- PFT bodybox: 4x
- Induced sputum : 5x
- CT Scan: 1-2x.
- Completing two questionnaires (BDI and TDI): 2x.
- Completion of a Diary: During entire study period.

Optional:
Additional blood collection for pharmacogenetic analysis: 1x

There are prohibited medications. See protocol section 5.5.9 page 63 for details.

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

Part 2 of protocol:
- Patients, smokers or ex-smokers with stable GOLD spirometry grades I-III COPD according to the current GOLD strategy (GOLD 2013). COPD is defined as patients with FEV1/FVC ratio *0.7 after bronchodilation.
- Current smokers with at least 10 pack years can be enrolled if they currently smoke *1ppd for last 3 months.
- A stable medical regimen for at least 4 weeks prior to screening.
- hsCRP * 1.5 mg/L at screening and baseline visit.
- Post-bronchodilator FEV1 at screening * 30% of predicted.
- Mean LCI 2.5% * 8 at screening.
- Evidence of air trapping on HRCT.
- Women of child bearing potential can be enrolled as long as they agree to use effective contraception (except hormonal contraceptives, due to the risk of drug-drug interaction with QBM076) as described in the protocol.

Exclusion criteria

Part 2 of protocol:
- Gold Class IV COPD
- Medication considered potential for DDI.
- Estimated CrCl < 30ml/min at screening.
- Serum creatinine *1.9 mg/dL at screening.
- More than 1 exacerbation requiring antibiotics or oral steroids in the 8 weeks prior to screening and/or hospitalization in 3 months prior to screening.
- History of malignancy within the past 5 years prior to screening.
- HRCT chest screen failure based on preset criteria for air trapping, emphysematous changes and extent of bronchiectasis

- Use of oral corticosteroids, theophylline (within 1 week prior to screening), PDE4 inhibitors or oral antibiotic use (e.g., macrolides).

Study design

Design

Study phase:	2
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):	07-05-2015
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	QBM076
Generic name:	QBM076

Ethics review

Approved WMO

Date:	22-12-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO

Date:	01-04-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-05-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2012-005615-92-NL
ClinicalTrials.gov	NCT01972776
CCMO	NL51583.058.14