A PHASE II, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF UK-432,097 DRY POWDER FOR INHALATION IN ADULTS WITH MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Primary ObjectiveTo evaluate the efficacy and safety/tolerability of UK-432,097 DPI in adults with moderate to severe COPD (GOLD stage II/III).

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

Summary

ID

NL-OMON30744

Source
ToetsingOnline

Brief title
Phase II study in adults with moderate to severe COPD.

Condition

- Bronchial disorders (excl neoplasms)

Synonym

COPD, Obstructive lung disease

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer

Intervention

Keyword: 097, COPD, Phase II, UK - 432

Outcome measures

Primary outcome

Change from baseline in trough (prior to administration of study drug) FEV1 at

Week 6.

Secondary outcome

Efficacy:

•Change from baseline in trough FEV1, forced expiratory volume in 6 seconds

(FEV6), forced vital capacity (FVC) and inspiratory capacity (IC) at weeks 2

and 4 and at week 8 (2 weeks after the completion of therapy).

• Change from baseline in trough FEV6, FVC and IC at week 6.

• Change from baseline in post-study drug FEV1, FEV6, FVC, and IC at weeks 2, 4

and 6.

• Change from baseline in post-bronchodilator FEV1, FEV6, FVC, and IC at week 6.

• Change from baseline in dyspnea (BDI/TDI) at weeks 2, 4 and 6.

• Change from baseline of COPD symptoms, rescue bronchodilator use (per daily diary) and peak expiratory flow rate (PEFR).

• Global impression of change (Clinician & Patient) at week 6.

Safety:

• Adverse events (AEs).

• Laboratory safety data.

• Change in vital signs (pulse & blood pressure) and ECG post study drug.

• Acute change in FEV1 post-study drug compared to pre-study drug.

Other:

• Population pharmacokinetics.

• Exploratory biomarkers (e.g. C reactive protein [CRP]).

Study description

Background summary

Options for pharmacological intervention in the treatment of COPD are limited. Short-acting and long-acting bronchodilators from both the β2-agonist and anti-cholinergic classes are available for the relief of bronchospasm associated with COPD, however no therapeutic class has consistently been shown to display anti-inflammatory properties across the spectrum of disease, with the use of inhaled corticosteroids (ICS) indicated only for subjects who frequently exacerbate, unlike in asthma where ICS are indicated for the maintenance treatment in all but the mildest and most intermittent subjects.

The development of an effective anti-inflammatory agent for COPD capable of maintaining clinical stability, optimally with attenuation in the rate of decline of lung function, would constitute a major advance in disease management.

UK-432,097 is an adenosine A2a receptor agonist that is being developed as an inhaled antiinflammatory agent for COPD. Adenosine A2a receptors are found on a range of human inflammatory cells including neutrophils and monocytes/macrophages. As UK-432,097 has been shown to inhibit the release of multiple neutrophil- and monocyte/macrophage - derived activation products from human cells ex vivo, this suggests that UK-432,097 may be effective as an anti-inflammatory agent for the treatment of COPD.

Study objective

Primary Objective

To evaluate the efficacy and safety/tolerability of UK-432,097 DPI in adults with moderate to severe COPD (GOLD stage II/III).

Study design

This is a 6 week, randomized, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of UK-432,097 DPI in adult subjects with moderate to severe COPD as defined by GOLD stages II-III.

The study comprises 9 clinic visits: a screening visit, 2 visits during the run-in phase (week -2 and week -1), a baseline/randomization visit (week 0) at the start of the double-blind treatment phase, 4 visits during the double-blind treatment phase (weeks 1, 2, 4 and 6) and a follow up visit (week 8) following a 2 week washout (run out) phase.

An interim analysis for efficacy will be performed based on the primary endpoint, namely mean change from baseline in trough FEV1 at week 6. This interim analysis will be triggered when approximately 80 subjects have completed double-blind treatment and the study may be terminated at that stage depending on a predefined stopping criteria based on futility

Intervention

Eligible subjects will be issued at screening with the short-acting bronchodilators, ipratropium bromide and salbutamol (albuterol) MDIs [supplied by Pfizer] and instructed in their use. These medications will be used throughout the study from screening through to week 8 (follow-up) and will be the only COPD medications allowed, with the exception of UK-432,097/placebo.

Study burden and risks

UK-432,097 is an adenosine A2a receptor agonist that is being developed as an inhaled antiinflammatory agent for COPD.
The development of an effective anti-inflammatory agent for COPD capable of maintaining clinical stability, optimally with attenuation in the rate of decline of lung function, would constitute a major advance in disease management.

The patient is asked to make the study visits and perform the study procedures according to protocol. The time the visits take is about 15 hours for each patient, for 9 study visits.

During these visits bloodsampling is done, ECGs are made and spirometries are done. See page 8-11 of the protocol for an overview of all trial procedures.

During the study all patients will be treated with salbutamol and ipratropium bromide. By randomisation will be determined whether a patient will be treated additionally with UK432,097 or placebo

Contacts

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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 subjects between, and including, the ages of 40 and 80 years. Females need to be of non-childbearing potential (criteria gespcificeerd).
2. Subjects with a diagnosis, for at least 6 months, of moderate to severe COPD (GOLD) and who meet the criteria for Stage II-III disease.
3. Subjects must have a smoking history of at least 10 pack-years* (criteria gespecificeerd).
4. Subjects must have stable disease for at least 1 month prior to screening.
5. Subjects must be able to give informed written consent prior to entering the study.

Exclusion criteria

1. More than 2 exacerbations of COPD requiring treatment with oral steroids in the preceding year or hospitalization for the treatment of COPD within 3 months of screening or more than twice during the preceding year.
2. History of a lower respiratory tract infection or significant disease instability during the month preceding screening or during the time between screening and randomization.
3. History or presence of respiratory failure, cor pulmonale or right ventricular failure.
4. Subjects with home oxygen therapy.
5. Any clearly documented history of adult asthma or other chronic respiratory disorders (e.g. bronchiectasis, pulmonary fibrosis, pneumoconiosis).
6. History of cancer (other than cutaneous basal cell) in the previous 5 years.
7. History within the previous year of: myocardial infarction, cardiac arrhythmia (e.g. atrial fibrillation, paroxysmal atrial fibrillation, atrial flutter, supraventricular tachycardia, ventricular tachycardia), left ventricular failure, unstable angina, coronary angioplasty, coronary artery bypass grafting (CABG) or cerebrovascular accident (including transient ischemic attacks)
8. A major surgical operation within 1 month of screening.
9. Screening systolic blood pressure < 90mmHg.

10. ECG abnormalities at screening or randomization (criteria specified).
11. Liver function test abnormalities (criteria specified)

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):	17-07-2007
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ipratropium bromide
Generic name:	Ipratropium bromide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Is er nog niet.
Generic name:	UK-432,097
Product type:	Medicine
Brand name:	Salbutamol sulphate
Generic name:	Albuterol sulphate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-01-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-02-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-02-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-04-2008
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
EudraCT	EUCTR2006-002578-23-NL
CCMO	NL14939.060.06