A phase III multicenter, randomized, parallel, controlled, double blind study to investigate the safety and efficacy of inhaled mannitol over 12 months in the treatment of bronchiectasis.

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2.1.1 Primary Objective:To evaluate the difference in the rates of graded pulmonary exacerbations in patients with bronchiectasis treated with inhaled mannitol compared with placebo control2.1.2 Secondary Objectives:EfficacyTo evaluate the...

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

Summary

ID

NL-OMON34341

Source
ToetsingOnline

Brief title
DPM-B-305

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Bronchiectasis

Research involving
Human

Sponsors and support

Primary sponsor: Pharmaxis Ltd
Source(s) of monetary or material Support: Opdrachtgever (industrie): Pharmaxis

Intervention

Keyword: Bronchiectasis, Mannitol

Outcome measures

Primary outcome

Primary Endpoint: Pulmonary exacerbation rates (graded exacerbations)

Secondary outcome

Secondary Endpoints:

Efficacy

St George*s Respiratory Questionnaire (SGRQ) scores

Courses of; days on and time to need for oral, IV or inhaled antibiotics

prescribed for worsening respiratory signs and symptoms related to a treated

pulmonary exacerbation

Time to first graded exacerbation; duration of graded exacerbations

24 hour sputum volume Change in daytime sleepiness scores

Change in FEV1, FVC, FEV1/FVC, FEF25-75 values (Exploratory) Number of

hospitalizations due to pulmonary exacerbations

Safety

Adverse events Airway reactivity following a mannitol tolerance test (MTT)

(acute decrease in FEV1 >20%) Laboratory tests: Complete blood count;

electrolytes; creatinine and blood urea nitrogen; and liver function tests

Qualitative sputum microbiology: disappearance or appearance of pathogens Vital signs

Costs, Health Status, Utilities and Cost Effectiveness

Total costs incurred in intervention and placebo control groups

* Costs associated with inhaled mannitol

* Costs of antibiotic use and rescue medication

* Costs of hospitalizations and other secondary care services used

* Cost of primary and community care services used Results from Health Utilities Index Questionnaire in intervention and placebo control groups to derive:

* Health status

* Health related quality of life

* Utility scores

* Calculation of quality adjusted life years Determination of cost-effectiveness ratios for intervention and placebo control groups

* Sensitivity analysis, to assess extent to which variation in parameter estimates affect cost effectiveness ratios

* Analysis on the extent to which variation in parameters affects results from the Health Utilities Index Questionnaire

Study description

Background summary

Bronchiectasis is a chronic lung condition in which damage to the airways causes abnormal dilation of one or more bronchi, leading to pooling of mucus in affected areas. Patients with bronchiectasis usually have cough and abnormal sputum production, some have wheeze and breathlessness. Undue tiredness and fatigue are often reported by patients with bronchiectasis. The increased production of mucus together with impairment of the mucociliary system leads to mucus accumulation, cough, sputum production and recurrent infections. Patients with mucociliary dysfunction are usually treated on a daily basis with physical treatment like postural drainage to help clear excessive secretions and also with pharmacological agents. However, the physico-chemical properties of the secretions from these patients are such that the currently available pharmacological and physical interventions are not very effective.
Inhaled dry powder mannitol is an osmotic agent that was first shown to increase mucociliary clearance in asthmatic and healthy subjects who have normal mucociliary clearance at baseline. It has been shown that a single inhalation of mannitol increases the clearance of mucus both acutely and over 24 hours in patients with bronchiectasis, and acutely in patients with cystic fibrosis. Clinical outcome studies have shown that inhaled mannitol over 2 weeks improves health related quality of life10 respiratory symptoms and fatigue, and respiratory symptoms, and daytime sleepiness11 in bronchiectasis patients. In addition, sputum collected from patients 1 hour post mannitol was shown to have physical changes that benefit mucus transport.

Study objective

2.1.1 Primary Objective:
To evaluate the difference in the rates of graded pulmonary exacerbations in patients with bronchiectasis treated with inhaled mannitol compared with placebo control

2.1.2 Secondary Objectives:
Efficacy
To evaluate the difference in Quality of Life as measured by the St. Georges Respiratory Questionnaire (SGRQ) in patients with bronchiectasis treated with inhaled mannitol compared with placebo control
To evaluate the difference in antibiotic use prescribed for treated pulmonary exacerbations in patients with bronchiectasis treated with inhaled mannitol compared with placebo control. Such antibiotic use parameters to be analyzed will include number of discrete courses; days on antibiotics; and time to antibiotic need.
To evaluate the difference in other graded exacerbation parameters (time to first exacerbation and duration of exacerbation) in patients with bronchiectasis treated with inhaled mannitol compared with placebo control
To evaluate the difference in sputum volume in patients with bronchiectasis treated with inhaled mannitol compared with placebo control
To evaluate the difference in daytime sleepiness scores in patients with bronchiectasis treated with inhaled mannitol compared with placebo control

To evaluate the difference in lung function (FEV1, FVC, FEV1/FVC, FEF25-75 values) in patients with bronchiectasis treated with inhaled mannitol compared with placebo control (Exploratory)
To investigate the difference in number of hospitalizations due to pulmonary exacerbations in patients with bronchiectasis treated with inhaled mannitol compared with placebo control

Safety
To monitor the safety profile of inhaled mannitol compared with placebo control in subjects with bronchiectasis by investigating adverse events, airway reactivity, hematology, clinical chemistry, sputum microbiology and vital signs

Costs, Health Status, Utilities and Cost Effectiveness
To compare health related costs of treating patients with bronchiectasis with inhaled mannitol and placebo control
To compare health status and utility scores in patients treated with inhaled mannitol compared with placebo control
To investigate health related quality of life (HRQL) and quality adjusted life years (QALYs) by treatment group using utility scores from the Health Utilities Index Questionnaire
To investigate cost effectiveness of treating patients with bronchiectasis with inhaled mannitol

Study design

This is a double-blind, randomized, parallel group, controlled, multi-center, interventional clinical trial in subjects with non-CF bronchiectasis.
Eligibility will be determined at Visit 0A & Visit 0B, and baseline assessments captured at Visit 0B prior to the mannitol tolerance test (MTT). Subjects must have a negative MTT result to be randomized. Randomized subjects will receive for 52 weeks, 400 mg BID inhaled mannitol or placebo control, in a ratio of 1:1. All subjects will be followed for 4 weeks following cessation of the intervention arm.

Intervention

Dose: 400mg inhaled mannitol BID or placebo control BID

Study burden and risks

See protocol: Time and Events schedule, p89 and section 'Known potential risks and benifits to human subjects', p16.

Contacts

Public
Pharmaxis Ltd

Unit 20 Rodborough
2086 French Forest NSW
AU
Scientific
Pharmaxis Ltd

Unit 20 Rodborough
2086 French Forest NSW
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Have given a written informed consent to participate in this study in accordance with local regulations
2. Confirmed diagnosis of (non-cystic fibrosis) bronchiectasis (diagnosed by CT, HRCT, or bronchogram)
3. Aged 18*85 years, male and female
4. FEV1 >40 and *85 % predicted and > 1.0L
5. Clinician documented history of at least 2 pulmonary exacerbations, each requiring antibiotic therapy, in the last 12 months prior to Visit 0A and a total of at least 4 in the last 2 years prior to Visit 0A
6. Total SGRQ score of *30 at Visit 0B
7. 24 hour sputum weight *10g at Visit 0B

Exclusion criteria

1. Have bronchiectasis as a consequence of cystic fibrosis or focal endobronchial lesion or otherwise curable causes (e.g. foreign body aspiration)
2. Be considered *terminally ill* or listed for transplantation
3. Be using hypertonic saline in the 14 days prior to commencing Visit 0B or thereafter at any time during the study
4. Have had rescue antibiotics in the 4 weeks prior to V0B (chronic background antibiotic therapy accepted)
5. Have smoked within the last 3 months and must not smoke during their participation in the study

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):	10-02-2011
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inhaled Dry Powder Mannitol
Generic name:	Inhaled Dry Powder Mannitol

Ethics review

Approved WMO Date:	22-10-2010
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	29-11-2010
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2008-008731-28-NL
ClinicalTrials.gov	NCT00669331
CCMO	NL33986.096.10