A randomised, multicentre, double-blind, placebo-controlled, crossover trial determining the efficacy of dry powder mannitol in improving lung function in subject with Cystic Fibrosis aged six to seventeen years.

Published: 02-10-2013
Last updated: 24-04-2024

The purpose of this trial is primarily to assess the efficacy of inhaled mannitol compared with a true placebo in subjects with cystic fibrosis aged 6 to 17 years.We hypothesize that inhaled mannitol will improve the overall health and hygiene of...

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

Summary

ID

NL-OMON39882

Source
ToetsingOnline

Brief title
DPM-CF-204

Condition

- Respiratory disorders congenital
- Congenital respiratory tract disorders

Synonym
mucoviscidosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cystic fibrosis, mannitol

Outcome measures

Primary outcome

To determine the effect of eight weeks of twice-daily treatment with inhaled

dry powder mannitol on lung function (FEV1) in subjects with CF who are aged

six to seventeen years

Secondary outcome

• To determine the effect of inhaled mannitol on FVC;

• To determine the effect of inhaled mannitol on FEF25-75 (exploratory

objective) and

• To assess the safety of inhaled mannitol.

• To evaluate the difference in treatment induced sputum weight in subjects

treated with inhaled mannitol compared to those treated with placebo.

Study description

Background summary

Inhaled mannitol is being developed as a therapeutic agent for the treatment of cystic fibrosis and other diseases characterized by difficult to clear, thickened respiratory mucus. The mucoactive effects of inhaled mannitol have been examined in several acute and short term studies and now warrant further

investigation.

Whilst paediatric and adolescent subjects (aged <18 years) have been studied in previous phase III clinical trials of inhaled mannitol that assessed improvements in lung function [10, 11], there are remaining uncertainties around the effect size of inhaled mannitol 400 mg b.d. in this population. While data from the previous phase III studies suggest the effect of the 400 mg dose was consistent across age groups, the 50 mg control groups also had some improvement in lung function in these age groups. Thus the effect size in these age groups remains unclear.

Different trials demonstrate the efficacy of mannitol:
-mannitol as bronchial provocation test
-mucociliary clearance studies in cystic fibrosis, bronchiectasis ans asthma
-therapeutic studies in bronchiectasis
-therapeutic studies in cystic fibrosis

Study objective

The purpose of this trial is primarily to assess the efficacy of inhaled mannitol compared with a true placebo in subjects with cystic fibrosis aged 6 to 17 years.

We hypothesize that inhaled mannitol will improve the overall health and hygiene of the lung through regular and effective clearing of the mucus load. On commencing treatment, we expect an acute clearance of the retained musus and with twice daily use, ongoing mucus clearance to be associated with reduced mucus production.

Study design

Randomised, multicentre, double-blind, placebo-controlled, crossover

Intervention

After satisfying all inclusion and exclusion criteria, subjects will be given a mannitol tolerance test (MTT). Those with a negative MTT result will be randomized to receive during 8 weeks B.D. 400mg of mannitol by inhalation or placebo. After a wash-out period of 8 weeks, subjects switch treatment for another 8 weeks period of time.

Study burden and risks

see flow-chart on page 6 of the protocol.
regarding the risks, please see ICF

Contacts

Public
Pharmaxis Limited

Rodborough road 20
Frenchs Forest NSW 2086
AU
Scientific
Pharmaxis Limited

Rodborough road 20
Frenchs Forest NSW 2086
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. personally provide, or have a legal guardian povide written informed consent to participate in the trial, according to local regulations;
2. RhDNase and maintenance antibiotic use is allowed but treatment must have been established at least 3 months prior to screening. The subject must remain on rhDNase and/or maintenance antibiotics for the duration of the trial. The subject must not commence treatment with rhDNase or maintenance antibiotics during the trial;
3. Have a confirmed diagnosis of cystic fibrosis (sweat test result >=60mEq/L chloride and/or genotyping showing two identifiable mutations consistent with a diagnosis of cystic fibrosis);
4. Be aged >= 6 years and < 18 years;
5. Have a percentage of predicted FEV1 of >=30% and <=90% at screening (visit 0). Percentage of predicted FEV1 will be calculated using Wang for children <8years, and using

NHanes III for those >=8 years; and
6. Be able to perform all the techniques necessary to measure lung function.

Exclusion criteria

1. be using maintenance nebulised hypertonic saline
2. be considered "terminally ill"; eligible for lung transplantation, or have received a lung transplant previously;
3. require home oxygen or assisted ventilation;
4. have had an episode of massive haemoptysis defined as acute bleeding >=240ml in a 24 hour period and/or recurrent bleeding >=100ml/day over several days in the three-months prior to screening (visit 0);
5. have a known intolerance to mannitol;
6. be taking non-selective beta-blockers;
7. in the three months prior to screening (visit 0) have had a myocardial infarction; a cerebral vascular accident; major ocular, abdominal, chest or brain surgery;
8. have a known cerebral, aortic or abdominal aneurysm;
9. be currently participating in, or have participated in another investigative drug trial within four weeks of screening (visit 0);
10. be pregnant or breastfeeding, or plan to become pregnant whilst in the trial;
11. for females of childbearing potential, be using an unreliable form of contraception (at the discretion of the investigator)
12. have any concomitant medical, psychiatric, or social condition that, in the investigator's opinion, would put the subject at significant risk, may confound the results or may significantly interfere with the subject's participation in the trial; or
13. have a 'failed' or 'incomplete' mannitol tolerance test

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):	20-05-2014
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dry powder mannitol for inhalation
Generic name:	Dry powder mannitol for inhalation
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-10-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2012-002699-14-NL
CCMO	NL41925.078.13