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Long-term efficacy and safety of Lamazym for the treatment of patients with alpha-Mannosidosis

Submission date
29/06/2012

Recruitment status
No longer recruiting

Registration date
29/06/2012

Overall study status
Completed

Last Edited
21/06/2019

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Alpha-mannosidosis is an inherited condition caused by a lack of alpha-mannosidase (LAMAN), an enzyme found inside then body's cells that normally breaks down complex sugars. Lack of this enzyme leads to a progressive loss of motor and mental ability. People of all ethnicities and both genders may be affected by the disease. The first symptoms are loss of hearing, coarse facial features, reduced mobility and mental retardation. The symptoms appear over time. Alpha-mannosidosis is very rare, affecting only 1 out of 1,000,000 people. Lamazym is an identical copy of the natural LAMAN enzyme. It is administered into the bloodstream to replace the LAMAN enzyme. Lamazym has been tested on animals with promising results but has been administered to people in only two studies. This study will test the long-term effect and safety of the drug in patients with alpha-mannosidosis.

Who can participate?
Patients with alpha-mannosidosis who participated in the previous two studies (EudraCT numbers 2010-022084-36 and 2010-022085-26).

What does the study involve?
All of the patients are treated with Lamazym infused directly into the bloodstream each week and the effects are assessed after about 3 and 6 months. Safety is tested by monitoring the patient's blood pressure, blood chemicals, production of antibodies, and side effects. The effectiveness is measured by monitoring the reduction of sugar chains in the blood and cerebrospinal (brain and spine) fluid. An MRI scan of the brain will be conducted, as well as a walking test, a lung function test, a hearing test, a movement test and a mental test. Once this study has been completed, if no safety issues arise, the patients are offered continued treatment until the product is available on the market.

What are the possible benefits and risks of participating?
As with most enzyme-replacement treatments, there is a possible risk of patients developing allergic and/or immune reactions to the enzyme. Animal studies and the first studies on human patients have not shown any serious side effects to the dose planned for patients in this study.

The patient's parents must inform the study staff if they observe anything unusual about the patient. The investigator will monitor any side effects that arise during the study and will take all relevant measures in order to treat any such reaction. The patient may experience discomfort after the catheter has been implanted in the bloodstream to help with treatment and the taking of blood samples (the patients will already have had this catheter implanted as part of the first study). MRI scanning of the brain will require general anaesthestic. Fasting before the MRI scan will therefore be necessary. Cerebrospinal fluid samples will be taken while the patient is anaesthetised. The taking of cerebrospinal fluid may cause headache. The movement test and the mental test will take some hours and may make the patient tired.

Where is the study run from?
The patients will be invited from hospitals all over Europe for treatment at the Copenhagen University Hospital (Rigshospitalet). It may also be possible for them to be treated at a hospital in /near their home countries.

When is the study starting and how long is it expected to run for?
June to July 2012.

Who is funding the study?
The study is financed by the EU.

Who is the main contact?
Laura Crowther
laura.crowther@cmft.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Miss Laura Crowther

Contact details
University Research Floor (5th Floor)
Royal Manchester Children's Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL
-
laura.crowther@cmft.nhs.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT01681940

Clinical Trials Information System (CTIS)
2011-004355-40

Protocol serial number
12605, rhLAMAN-04

Study information

Scientific Title
A multicenter, open-label trial of the long-term efficacy and safety of Lamazym for the treatment of patients with alpha-Mannosidosis

Study objectives
Alpha-Mannosidosis is a rare lysosomal storage disorder caused by deficiency of the lysosomal enzyme alphamannosidase. The effect of the enzyme deficiency is accumulation of mannoserich glycoproteins in the tissues. It is inherited in an autosomal recessive manner. The typical symptoms include facial characteristics, mental retardation, ataxia, hearing impairment, impaired speech, recurrent infections, skeletal abnormalities, muscular pain and weakness.

There is a slow progression of symptoms over several decades. The longterm prognosis is generally poor. The clinical variation is considerable, encompassing a continuum from mild to severe. Most of the patients are diagnosed in their first or second decade of life. Increased levels of mannoserich oligosaccharides in urine, reduced activity of alphamannosidase in leukocytes and finding of two pathogenic mutations in MAN2B1 identify the patients. Currently no effective clinical treatment for alpha-Mannosidosis exists. Medical treatments are confined to be supportive and symptomatic. Lamazym is recombinant human lysosomal alpha-Mannosidase developed as an intravenous enzyme replacement therapy (ERT) for the treatment of alphaMannosidosis.

The current trial is being performed to evaluate the long-term efficacy, safety and tolerability of Lamazym treatment in patients with alpha-Mannosidosis. If successful, the enzyme replacement therapy is expected to be given lifelong, with the aim of normalizing the mannoserich oligosaccharide levels in the tissues, altering the progression of the disease and thereby preventing or reducing abnormalities from being developed and hopefully improving the patient's condition and quality of life.

Ethics approval required
Old ethics approval format

Ethics approval(s)
12/NW/0119

Primary study design
Interventional

Study design
Non-randomised; Interventional; Design type: Treatment

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Medicines for Children Research Network; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
Infusion of Lamazym 1 mg/kg given weekly for 6 months

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Lamazyn

Primary outcome(s)
Reduction of Oligosaccharides in blood serum and cerebrospinal fluid (CSF) and an improvement in the 3 minute stair climb

Key secondary outcome(s)
No secondary outcome measures

Completion date
31/07/2012

Eligibility

Key inclusion criteria
1. The subject must have participated in the phase 1 trial (EudraCT number: 201002208436) and phase 2a trial (EudraCT number: 201002208526)
2. Subject or subjects legally authorized guardian(s) must provide signed, informed consent prior to performing any trial related activities (trial related activities are any procedures that would not have been performed during normal management of the subject)
3. The subject and his/her guardian(s) must have the ability to comply with the protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Total final enrolment
10

Key exclusion criteria
1. The subject cannot walk without support
2. Presence of known chromosomal abnormality and syndromes affecting psychomotor

development, other than alphaMannosidosis
3. History of bone marrow transplantation
4. Presence of known clinically significant cardiovascular, hepatic, pulmonary or renal disease or other medical conditions that, in the opinion of the Investigator, would preclude participation in the trial
5. Any other medical condition or serious intercurrent illness, or extenuating circumstance that, in the opinion of the investigator, would preclude participation in the trial
6. Pregnancy
7. Psychosis within the last 3 months
8. Planned major surgery that, in the opinion of the investigator, would preclude participation in the trial
9. Participation in other interventional trials testing IMP except for studies with Lamazym

Date of first enrolment
22/06/2012

Date of final enrolment
31/07/2012

Locations

Countries of recruitment
United Kingdom

England

Belgium

Denmark

France

Germany

Poland

Spain

Study participating centre
Royal Manchester Children's Hospital
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
Royal Manchester Children's Hospital (UK)

ROR
https://ror.org/052vjje65

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			21/06/2019	No	No
HRA research summary			28/06/2023	No	No