A PHASE 4 PROSPECTIVE EXPLORATORY MUSCLE BIOPSY, BIOMARKER, AND IMAGING ASSESSMENT STUDY IN PATIENTS WITH LATE-ONSET POMPE DISEASE TREATED WITH ALGLUCOSIDASE ALFA.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Inborn errors of metabolism
Study type	Interventional

Summary

ID

NL-OMON39502

Source
ToetsingOnline

Brief title
Exploratory Muscle Biopsy Assessment Study (EMBASSY)

Condition

- Inborn errors of metabolism

Synonym
acid alfa glucosidase deficiency, Pompe disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Alglucosidase Alfa, Biomarkers, Muscle biopsy, Pompe disease

Outcome measures

Primary outcome

The primary endpoint of this study is: Percent reduction from baseline in

tissue glycogen content in muscle biopsy samples at Week 26.

Secondary outcome

The secondary endpoints of this study are:

- Tissue examination (to include assessment of glycogen distribution, muscle

fiber morphology, and lysosomal inclusions).

- Qualitative assessment of MR images for intact muscle and fatty replacement.

Study description

Background summary

Pompe disease is a rare, inherited disease caused by the deficiency of the enzyme acid α-glucosidase. This enzyme normally breaks down sugar stored as glycogen into glucose that can be used for energy by the body*s cells. If the enzyme is not present, glycogen builds up in certain tissues, particularly the muscles, including the heart and diaphragm (the main breathing muscle under the lungs). The progressive build-up of glycogen causes a wide range of symptoms, including an enlarged heart, breathing difficulties and muscle weakness. The disease can appear at birth (the *infantile-onset* form) but also later in life (the *late-onset* form).Alglucosidase alfa has been developed as an enzyme replacement therapy for the treatment of Pompe disease and is registered since 2006.

Currently, there is no validated, sensitive non-invasive or minimally invasive biomarker to monitor alglucosidase alfa pharmacodynamics in patients with late-onset Pompe disease. Limited pathological data from late-onset patients suggests significant patient to patient heterogeneity in terms of disease severity. As a result, this study aims to explore the feasibility of using MRI imaging and selective confirmatory muscle biopsy to characterize disease burden and response to treatment with alglucosidase alfa in patients with late-onset Pompe disease.

Study objective

Primary Objective
The primary objective of this study is to evaluate glycogen clearance in muscle tissue samples collected pre and post alglucosidase alfa treatment in patients with late-onset Pompe disease.

Secondary Objectives
The secondary objectives of this study are:

to characterize the disease burden in patients with late-onset Pompe disease and explore imaging, histologic, and functional assessments in these patients.

to explore potential plasma or urine biomarkers relative to late-onset Pompe disease and patient*s response to treatment with alglucosidase alfa.

Study design

Phase 4 prospective exploratory open-label multicenter study

Intervention

All patients receive every 2 weeks an intravenous infusion for 24 weeks of alfa glucosidase alfa, a medication used for Pompe's disease.

Study burden and risks

Risks
• Functional testing: falls, shortness of breath, muscle soreness, and fatigue
• Repeat blood draws: momentary discomfort, bruising, excessive bleeding, infection, fainting, and possible anemia
• Biopsy: soreness, infection, bleeding, bruising, and scarring at the biopsy site
• MRI: claustrophobia in some patients, no physical risk
• Administration of medications:
About half of the infantile-onset patients who received the study drug in clinical trials experienced infusion reactions to study drug. One third of the

late-onset patients experienced infusion reactions to study drug. Infusion reactions occur at any time during, and within a few hours after the infusion and are more likely with higher infusion rates. The majority of reactions were assessed as mild to moderate and resolved spontaneously. In a previous study, infusion reactions which were reported in at least 5 out of 100 late-onset patients treated with study drug included headache, nausea, dizziness, hives, rash, chest discomfort, vomiting, sweating, flushing (red in the face) and blood pressure increased. Less commonly, approximately 2 out of 100 patients can experience infusion reaction that can be life-threatening; this is known as an anaphylactic reaction or severe allergic reaction.

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.
The patient is willing and able to provide signed informed consent.
2.
The patient is >=18 years of age with confirmed acid α-glucosidase [GAA] enzyme deficiency from any tissue source and/or confirmed GAA gene mutations and without known cardiac hypertrophy.
3.
The patient is able to ambulate a certain distance without stopping and without an assistive device. Use of assistive device for community ambulation is appropriate.
4.
The patient has a certain forced vital capacity (FVC) in upright position.
5.
The patient, if female and of childbearing potential, must have a negative pregnancy test at baseline. Note: All female patients of childbearing potential and sexually mature males must agree to use a medically accepted method of contraception throughout the study.

Exclusion criteria

1.
The patient has had previous treatment with Enzyme Replacement Therapy.
2.
The patient is wheelchair dependent.
3.
The patient requires invasive-ventilation (non-invasive ventilation is allowed).
4.
The patient is participating in another clinical study using investigational treatment.
5.
The patient cannot submit to MRI examination because of a formal contraindication such as a pacemaker, implanted ferromagnetic metals, etc.
6.
The patient, in the opinion of the Investigator, is unable to adhere to the requirements of the study.

Study design

Design

Study phase:	4
Study type:	Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-01-2012
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Myozyme
Generic name:	Alglucosidase Alfa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-08-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-11-2012

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-04-2013
Application type:	Amendment
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	EUCTR2010-020611-36-NL
ClinicalTrials.gov	NCT01288027
CCMO	NL37650.078.11