A Phase 3 Randomized, Multicenter, Multinational, Double-blinded Study Comparing the Efficacy and Safety of Repeated Biweekly Infusions of NeoGAA (GZ402666) and Alglucosidase Alfa in Treatment naïve Patients with Late-onset Pompe Disease

Published: 15-06-2016
Last updated: 31-12-2024

The overall objective of this study is to evaluate the efficacy and safety of neoGAA in treatment-naïve patients with LOPD as compared to alglucosidase alfa, when this is administered biweekly for a period of 49 weeks. Also, there is an open-label...

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

Summary

ID

NL-OMON46174

Source
ToetsingOnline

Brief title
COMET

Condition

- Inborn errors of metabolism

Synonym
acid alfa glucosidase deficiency, Pompe Disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: efficacy, neoGAA, Phase III, Pompe Disease

Outcome measures

Primary outcome

Change in FVC % predicted in the upright position from baseline to

12 months.

Secondary outcome

Change in the following parameters from baseline to 12 months:

Efficacy:

• MIP and MEP (% predicted)

• 6MWT distance walked

• Motor function (QMFT)

• Muscle strength (HHD)

• Health-related quality of life (SF-12)

Study description

Background summary

Pompe disease is a rare, inherited disease caused by the deficiency of the enzyme acid alfa-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 muscles, including the heart and the diaphragm (the main breathing muscle under the lungs). The progressive build up of glycogen causes a wide reange 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).

Study objective

The overall objective of this study is to evaluate the efficacy and safety of neoGAA in treatment-naïve patients with LOPD as compared to alglucosidase alfa, when this is administered biweekly for a period of 49 weeks. Also, there is an open-label follow up included, to measure the long term effects of neoGAA administration.

Study design

A phase 3 randomized, multicenter, multinational study with a double-blinded treatment phase, followed by an open-label follow up phase.

Intervention

biweekly intravenous injections with neoGAA or alfa glucosidase, in a dose of 20 mg/kg.
After 49 weeks all patients will receive neoGAA 20 mg/kg for the remaining period of the study.

Study burden and risks

24 patients were treated in the TDR12857 study, and results showed effectiveness and an expected safety profile of neoGAA in Pompe patients.

Risks
• Functional testing: falls, shortness of breath, muscle soreness, and fatigue
• Repeat blood draws: momentary discomfort, bruising, excessive bleeding, infection, fainting, and possible anemia. According to the WHO criteria, the blood draws are classified as minimal risk (Howie, SRC. Bull World Health Organ 2011; 89:46-53).
-questionnaires: these are quality of life related and Pompe disease. Children will receive special questionnaires.
• Administration of medications:
So far 24 patients were treated with neoGAA, and the extension study (LTS13769) is still running in which all patients receive 20 mg/kg neoGAA.
8 out of 24 patients received and infusion reaction. Most of these reactions were mild to moderate and resolved spontaneously, except for one patient whom

experienced a severe allergic reaction with respiratory problems and chest pressure.
The most common side effect was headache (10 patients out of 24), then fatigue and muscle pain (6 patients out of 24 each) and redness (3 out of 24 patients).

About one third of the adults with Pompe disease experience infusion reactions during or after the infusion with Myozyme. The majority of the reactions are characterized as mild to moderately sever and resolved spontaneously.

The most common infusion reactions from NeoGAA are:

- difficulty breathing, abnormal breathing sounds
- swelling of the lips and tongue,
- throat pressure.
- chest pressure,
- abnormal heart beating
- caughing,
- redness, itch and redness of the face
- generalized rash
- dizziness, drop in bloodpressure
- nausea,
- acid reflux
- skin reaction at infusion site,
- headache,
- muscle ache

Contacts

Public
Sanofi-aventis

Kampenringweg 45E
Gouda 2803PE
NL
Scientific
Sanofi-aventis

Kampenringweg 45E
Gouda 2803PE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

-The patient has confirmed GAA enzyme deficiency from any tissue source and/or 2 confirmed GAA gene mutations
-The patient and/or their parent/legal guardian is willing and able to provide signed informedconsent, and the patient, if <18 years of age, is willing to provide assent if deemed able to do so.
-The patient (and patient*s legal guardian if patient is <18 years of age) must have the ability to
comply with the clinical protocol.
-The patient, if female and of childbearing potential, must have a negative pregnancy test (betahuman
chorionic gonadotropin) at baseline.

Exclusion criteria

-The patient is younger than 3 years of age.;-The patient has known Pompe specific cardiac hypertrophy.;-The patient is wheelchair dependent.;-The patient is not able to ambulate 40 meters (approximately 130 feet) without topping and without an assistive device.;-The patient requires invasive-ventilation (non-invasive ventilation is allowed).;-The patient is not able to successfully perform repeated forced vital capacity (FVC) measurements in upright position of >=40% predicted and <=85% predicted.;-The patient has had previous treatment with alglucosidase alfa or any investigational therapy for Pompe disease.;-The patient has prior or current use of immune tolerance induction therapy.

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:	Completed
Start date (anticipated):	15-05-2017
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Myozyme/Lumizyme
Generic name:	alglucosidase alfa
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	neoGAA

Ethics review

Approved WMO

Date:	15-06-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	21-03-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-10-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-05-2018
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	15-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-10-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2022
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	EUCTR2016-000942-77-NL
CCMO	NL57636.078.16
Other	zie sectie J

Study results

Date completed:	02-08-2022
Results posted:	05-12-2023

First publication
15-11-2023