An Open-label, Multinational, Multicenter, Intravenous Infusion Study of the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of avalglucosidase alfa in Treatment-naïve Pediatric Participants with Infantile-Onset Pompe Disease (IOPD)

Published: 04-05-2021
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This study has been transitioned to CTIS with ID 2024-513859-33-00 check the CTIS register for the current data. The overall objective is to assess efficacy, safety, pharmacokinetic (PK), pharmacodynamics (PD) of avalglucosidase alfa in male and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON52076

Source
ToetsingOnline

Brief title
baby-COMET

Condition

- Metabolic and nutritional disorders congenital

Synonym
acid alpha glucosidase deficiency, Pompe Disease

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Sanofi B.V.

Intervention

Keyword: Avalglucosidase alfa, Efficacy, Phase III, Pompe Disease

Outcome measures

Primary outcome

To determine the effect of avalglucosidase alfa treatment on survival and invasive ventilator-free survival of IOPD participants after 52 weeks of treatment.

Secondary outcome

To determine the effect of avalglucosidase alfa treatment on survival and invasive ventilator-free survival at 12 and 18 months of age, as well the change in left ventricular mass Z-score (LVM Zscore); Alberta Infant Motor Scale (AIMS) score; body length, body weight, and head circumference Z-scores; and urinary Hex4 at Week 52

To determine safety, tolerability, and immunogenicity of avalglucosidase alfa

To determine the PK profile at Week 12 and Week 52

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 range of symptoms, including an enlarged heart and 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

This study has been transitioned to CTIS with ID 2024-513859-33-00 check the CTIS register for the current data.

The overall objective is to assess efficacy, safety, pharmacokinetic (PK), pharmacodynamics (PD) of avalglucosidase alfa in male and female participants less than or equal to 6 months of age with IOPD.

Study design

This is a single group, treatment, Phase 3, open-label study to assess efficacy, safety, pharmacokinetic (PK), pharmacodynamics (PD) of avalglucosidase alfa in male and female participants less than or equal to 6 months of age with IOPD.
The study will also include up to 2 participants 7 to 12 months of age to be evaluated combined and seperately with participants <6 months of age.
Following a screening period of up to 4 weeks, all participants will be treated with avalglucosidase alfa 40 mg/kg qow for 52 weeks for the PAP and will continue to receive treatment in the subsequent 52-week study ETP. This will be followed by an ELTP up to 104 weeks plus the 4-week follow-up for a total study duration of up to 4.08 years.

Intervention

Biweekly intravenous injections with avalglucosidase alfa in a dose of 40 mg/kg. This can be increased to weekly dosing of 40 mg/ kg is needed for safety or efficacy reason,

Study burden and risks

Risks
- Functional testing: Fatigue
- Blood draws: momentary discomfort, swelling, bruising, infection, bleeding, pain, light-heaed, redness at injection site. If possible a central venous catheter will be placed for blood collection to reduce pain by needle sticks.
- Elecrocardiogram (ECG): momentary discomfort
- Administration of medication
Infusion associated reaction occurred at patients receiving avalglucosidase alfa:
- Very common (affecting more than 1 in 10 people):
headache, generalized rash, muscle pain, nausea, diarrhea

- Common, frequent (affecting up to 1 in 10 people) :
redness, cough, dizziness, difficulty breathing, acid reflux, chest pressure, decreased blood pressure, itching, feeling tired, feeling hot, feeling cold or having chills, swelling of face, lip and tongue, arms or legs, throat tightness**infusion site reaction**abnormal breathing sounds**abnormal heart beating**redness in the face

Other possible side effects seen in both infantile- and/or late-onset patients treated with avalglucosidase (affecting more than 1 in 10 people):
nasopharyngitis, headache, diarrhoea, back pain, fall, nausea, pain in extremity, upper respiratory tract infection, rash, arthralgia, influenza, fatigue, vomiting, myalgia, muscle spasms, pyrexia, dizziness, musculoskeletal pain, pruritus, abdominal pain, contusion

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

- Participants must have confirmed diagnosis of infantile-onset Pompe disease defined as:
the presence of 2 lysosomal acid α-glucosidase (GAA) pathogenic variants and a documented GAA deficiency from blood, skin, or muscle tissue; or the presence of 1 GAA
pathogenic variant and a documented GAA deficiency from blood, skin and muscle tissue
in 2 separate samples (from either 2 different tissues or from the same tissue but at 2
different sampling dates).
- Participants must have established cross-reactive immunological material (CRIM) status
available prior to enrollment.
- Participants must have cardiomyopathy at the time of diagnosis: ie, LVMI equivalent to
mean age specific LVMI
+1 standard deviation for participants diagnosed by newborn screening or sibling screening;
+2 standard deviation for participants diagnosed by clinical evaluation.
- Parents or legally authorized representative(s) must be capable of giving signed
informed consent.

Exclusion criteria

- Participants with symptoms of respiratory insufficiency, including any ventilation use

(invasive or noninvasive) at the time of enrollment.
- Participants with major congenital abnormality.
- Participants with clinically significant organic disease (with the exception of symptoms
relating to Pompe disease).
- Participant received enzyme-replacement therapy (ERT) with recombinant human acid α
glucosidase (rhGAA) from any source.
- Participant who has previously been treated in any clinical trial of avalglucosidase alfa.
- Participant not suitable for participation, whatever the reason, as judged by the
Investigator, including medical or clinical conditions, or participants potentially at risk of
noncompliance to study procedures.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	31-05-2021
Enrollment:	1
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	avalglucosidase alfa

Ethics review

Approved WMO Date:	04-05-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-10-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	04-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	24-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Not approved

Date:	26-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	09-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Not approved

Date:	21-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	15-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	25-04-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	21-06-2024
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
EU-CTR	CTIS2024-513859-33-00
EudraCT	EUCTR2020-004686-39-NL
ClinicalTrials.gov	NCT04910776
CCMO	NL76557.078.21