A randomized, open-label, parallel-group, 18-month Phase 3 study to evaluate the effect of venglustat compared with usual standard of care on left ventricular mass index in participants with Fabry disease and left ventricular hypertrophy

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This study has been transitioned to CTIS with ID 2023-509715-91-00 check the CTIS register for the current data. Primary:•To compare the effect of venglustat with standard of care Fabry therapies on left ventricular mass index over 18 months in...

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

Summary

ID

NL-OMON54374

Source
ToetsingOnline

Brief title
EFC16158 CARAT

Condition

- Inborn errors of metabolism

Synonym
Fabry disease, heart failure

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Fabry, Phase 3, Venglustat

Outcome measures

Primary outcome

-Slope of left ventricular mass index as measured by cardiac magnetic resonance imaging (MRI) (central reading).

Secondary outcome

• Slope of estimated glomerular filtration rate (eGFR) as assessed by the chronic kidney disease epidemiology collaboration (CKD-EPI) creatinine equation

• Change in T1 relaxation time, measured by cardiac MRI (central reading)

• Change in global longitudinal strain, measured by echocardiography (central reading)

• Percent change in tiredness component of FD-PRO

• Percent change in swelling in lower extremities component of FD-PRO

• Change in the lens clarity by ophthalmological examination

• Number of participants with adverse event (AE) and serious adverse event (SAE)

• Change in Beck Depression Inventory-II (BDI-II) score

• Plasma venglustat concentrations at prespecified visits over the study duration

Study description

Background summary

A randomized, open-label, parallel-group, 18-month Phase 3 study to evaluate the effect of venglustat compared with usual standard of care on left ventricular mass index in participants with Fabry disease and left ventricular hypertrophy.

The study consists of two different parts, a randomization period and an open label period.

Study objective

This study has been transitioned to CTIS with ID 2023-509715-91-00 check the CTIS register for the current data.

Primary:
•To compare the effect of venglustat with standard of care Fabry therapies on left ventricular mass index over 18 months in participants with Fabry disease and left ventricular hypertrophy
Secondary:
•To evaluate the effect of venglustat on renal function
•To evaluate the effect of venglustat versus standard therapy on measures of cardiac function and cardiac lipid storage
•To evaluate the effect of venglustat on lower extremities swelling and tiredness
•To assess the safety and tolerability of venglustat in participants with Fabry disease
•To evaluate the PK of venglustat in participants with Fabry disease

Study design

Randomized, open-label, Phase 3, multi center.

Intervention

Investigational drugs: Venglustat
Pharmaceutical form: tablet
Route of administration: oral

Fabryzyme according to SoC.

Study burden and risks

The risk are related to blood withdrawal, MRI scans of the heart, intake of the investigational drugs and possible side effects of the investigational drugs.

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

-Male and female participants aged 18 to 65 with previously confirmed diagnosis of Fabry
disease and a history of clinical symptoms of Fabry disease.
-Participants may be receiving treatment with agalsidase alfa, agalsidase beta, or
migalastat, or may be untreated.
-Left ventricular hypertrophy.
-Contraception for male or female participants: not pregnant or breastfeeding;

no sperm
donating for male participant.
-A signed informed consent must be provided prior to any study-related procedures.

Exclusion criteria

-History of transient ischemic attack, stroke, myocardial infarction, heart failure, major cardiovascular surgery or kidney transplantation.
-History of seizures currently requiring treatment.
-Underlying medical condition that may cause or contribute to left ventricular hypertrophy.
-Asymmetric hypertrophy by cardiac MRI at screening if considered by central reader to be not related to Fabry disease.
-Advanced cardiac fibrosis, defined as significant late gadolinium enhancement affecting 3 or more segments involving > 50% of myocardial thickness on screening cardiac MRI.
-History of clinically significant cardiac arrhythmia. Atrial fibrillation that is well controlled on a stable medical regimen for at least 12 months is not an exclusion if the CHA2DS2-VASc score is 0 for males or 1 for females.
-Estimated glomerular filtration rate <60 mL/min/1.73m2.
-Presence of severe depression as measured by Beck*s Depression Inventory (BDI)-II >28
and/or a history of an untreated, unstable major affective disorder within 1 year of the
screening visit.
-Patients with hepatitis C, HIV, or hepatitis B infection.
-Positive SARS-CoV-2 virus test within 2 weeks of enrollment, or COVID-19 requiring
hospitalization within 6 months of enrollment.
-History of drug and/or alcohol abuse.
-Moderate to severe hepatic impairment.
-History of or active hepatobiliary disease.
-Liver enzymes (alanine aminotransferase/aspartate aminotransferase) or total bilirubin
>2 times the upper limit of normal.
-Strong or moderate inducers or inhibitors of cytochrome P450 CYP3A4 within 14 days or 5 half-lives, whichever is longer,
prior to randomization.
- Known contraindication to undergoing MRI or known hypersensitivity to gadolinium-based contrast agents.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-05-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Agalsidase beta
Generic name:	Fabrazyme®
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Venglustat
Generic name:	NA

Ethics review

Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2022

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	07-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	30-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	13-06-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	19-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	2021-002320-20
EU-CTR	CTIS2023-509715-91-00
EudraCT	EUCTR2021-002320-20-NL
CCMO	NL79008.018.21