Open label, Two Cohort (with and without Imiglucerase), Multicenter Study to Evaluate Pharmacokinetics, Safety, and Efficacy of Eliglustat in Pediatric Patients with Gaucher Disease Type 1 and Type 3

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The purpose of this study is to evaluate the possible risks and efficacy (improvement of disease) with an experimental oral study drug named eliglustat in pediatric patients from 2 to 18 years with Gaucher disease.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48873

Source
ToetsingOnline

Brief title
ELIKIDS

Condition

- Other condition
- Metabolic and nutritional disorders congenital

Synonym
Gaucher disease; lysosomal storage disease

Health condition

erfelijke lysosomale stofwisselingsziekte (Gaucher)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: children, eliglustat, Gaucher disease, imiglucerase

Outcome measures

Primary outcome

Evaluate the safety and pharmacokinetics of eliglustat in pediatric patients (2

to 18 years old).

Secondary outcome

Evaluate the efficacy of eliglustat and quality of life in pediatric patients

(2 to 18 years old).

Study description

Background summary

Gaucher disease is caused by not having the normal amount of an enzyme called acid β-glucosidase. This enzyme*s role is to breakdown lipids, a fatty substance in the body, called glucosylceramide. As time goes by, cells become overloaded with glucosylceramide and become injured. This can lead to an enlarged liver and spleen, bone problems as well as other symptoms such as trouble breathing, reduced amount of healthy red blood cells and platelets (blood clotting cells), tiredness, and sometimes bleeding.

Study objective

The purpose of this study is to evaluate the possible risks and efficacy (improvement of disease) with an experimental oral study drug named eliglustat in pediatric patients from 2 to 18 years with Gaucher disease.

Study design

Fase 3, open label, 2 treatment arms with eliglustat and imiglucerase.

Intervention

- Cohort 1: Eliglustat monotherapy: Eliglustat for two years. Cohort 1 patients that experience significant clinical decline will receive rescue treatment. Rescue Treatment Step 1: Switch from eliglustat to imiglucerase monotherapy. Rescue treatment Step 2: Patients who after 6 months of rescue therapy with imiglucerase monotherapy do not show improvement in the parameter(s) that led to the switch from eliglustat to imiglucerase, will then receive combination therapy with eliglustat + imiglucerase

- Cohort 2: Eliglustat plus imiglucerase Eliglustat plus imiglucerase for two years, at the dose of enzyme replacement therapy received before enrollment. After Week 52, Cohort 2 patients will switch to eliglustat monotherapy for the remainder of the study if the desired clinical response has been achieved.

Study burden and risks

Risks and burdens related to blood collection, study procedures and possible adverse events.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

-The patient is 6 to <18 years old at the time of informed consent.
-Male and female patients with a clinical diagnosis of Gaucher disease (GD) type 1 or type 3 with documented deficiency of acid beta-glucosidase activity by enzyme assay and glucocerebrosidase (GBA) genotype.
-Postmenarchal female patients must have a documented negative pregnancy test prior to enrollment and throughout the study. Patients must be willing to practice true abstinence in line with their preferred and usual lifestyle, or use a medically accepted form of contraception throughout the study.;Cohort 1 (Eliglustat monotherapy):
-Patients must have been receiving an enzyme replacement therapy (ERT) for a minimum of 24 months at a monthly dose equivalent to 30 U/kg to 130 U/kg of Cerezyme® (imiglucerase) with treatment ongoing at the time of enrollment. Patients must be at pre-specified treatment goals, as defined by:
-Hemoglobin level for ages 6 to <12 years: >=11.0 g/dL; for ages 12 to <18 years: >=11.0 g/dL for females and >=12.0 g/dL for males;
-Platelet count >=100,000/mm3;
-Spleen volume <10.0 multiples of normal (MN);
-Liver volume <1.5 MN;
-Absence of GD related pulmonary disease, and severe bone disease, as defined below for Cohort 2.;Cohort 2 (Eliglustat plus imiglucerase):
-Patients must have been receiving an ERT for a minimum of 36 months at a dose equivalent to at least 60 U/kg of imiglucerase every 2 weeks at the time of enrollment with treatment ongoing at the time of enrollment and the dose stable for at least the 6 months preceding enrollment. Patients must have severe clinical manifestations of GD, as defined by the presence of at least of the following:
-GD related pulmonary disease such as interstitial lung disease (ILD). The diagnosis of ILD must be confirmed by the presence of reticulonodular densities on chest X-ray.
AND/OR
-Symptomatic bone disease characterized by pathological fracture, osteonecrosis, osteopenia/osteoporosis, or bone crisis occurring in the 12 months prior to enrollment.
AND/OR

-Persistent thrombocytopenia (<80,000/mm3) related to GD.

Exclusion criteria

-Substrate reduction therapy for GD within 6 months prior to enrollment
-Partial or total splenectomy if performed within 2 years prior to enrollment
-The patient is transfusion dependent, a history of esophageal varices or liver infarction, elevated liver enzymes, significant congenital cardiac defect, coronary artery disease or left sided heart failure; clinically significant arrhythmias or conduction defect such as Type 2 second degree or third degree atrioventricular (AV) block, complete bundle branch block, prolonged QTc interval, or sustained ventricular tachycardia (VT).
-The patient has any clinically significant disease other than GD.
-The patient has neurological symptoms other than oculomotor apraxia at study entry.
-The patient has received an investigational product within 30 days prior to enrollment.
-The patient is unable to receive treatment with imiglucerase due to a known hypersensitivity or is unwilling to receive imiglucerase treatment every 2 weeks.
-The patient has a known hereditary galactose intolerance, Lapp lactase deficiency or glucose galactose malabsorption, or is a CYP2D6 ultra-rapid metabolizer or indeterminate metabolizer.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Cerdelga
Generic name:	Eliglustat
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cerezyme
Generic name:	Imiglucerase
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-06-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2019
Application type:	First submission
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	2016-000301-37

Register	ID
EudraCT	EUCTR2016-000301-37-NL
CCMO	NL65913.018.18