Clinical Survey Study to Assess Physical Function and the Incidence of Hypoglycemia in Patients 1 Year of Age and Over with GSD III.

Published: 10-08-2022
Last updated: 17-01-2025

The primary objective of this study is to evaluate the incidence of hypoglycemia in adult and pediatric patients with GSD III. The secondary objective of this study is to evaluate the sensitivity of various muscle strength and function measures to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON51818

Source
ToetsingOnline

Brief title
UX053-CL002

Condition

- Metabolic and nutritional disorders congenital

Synonym
Glycogen Storage Disease III

Research involving
Human

Sponsors and support

Primary sponsor: Ultragenyx pharmaceutical Inc.

Source(s) of monetary or material Support: industry

Intervention

Keyword: Glycogen, GSDIII, Storage Disease

Outcome measures

Primary outcome

The primary endpoint of this study is the incidence of hypoglycemia during the

26-week Observation Period.

Secondary outcome

Additional details regarding the primary analysis are in the Statistical

Analysis Plan (SAP)

Study description

Background summary

Glycogen Storage Diseases represent a group of metabolic disorders in which there is a deficiency in the function of enzymes required to metabolize glycogen, including synthesis, degradation, or regulation of glycogen. Glycogen is the stored form of glucose, with glycogen formation occurring with carbohydrate loading and glycogen degradation (glycogenolysis) to glucose occurring to provide immediate energy and maintain blood glucose levels. GSD III is a rare, autosomal recessive, metabolic disease, characterized by a broad spectrum of clinical manifestations affecting primarily the liver, cardiac muscle, and skeletal muscle. Other names for GSD III include limit dextrinosis disease, Cori disease, and Forbes disease.

Clinical characteristics vary depending on the relative extent of liver or muscle involvement, with most patients experiencing consequences of both liver and muscle involvement . Patients with GSD III generally present by the age of 1.5 years with hepatomegaly, the most common presenting clinical sign. Other hallmarks of the disease include ketotic hypoglycemia with fasting, hyperlipidemia, growth retardation, elevated liver transaminases, and elevated creatine kinase. Some individuals also develop osteoporosis or osteopenia over time . Hepatomegaly may appear to improve with age with a reduced relative glucose requirement; however, it is increasingly recognized that progressive

liver cirrhosis and hepatic failure can occur, with some patients developing hepatic adenoma, hepatocellular carcinoma, or end-stage liver cirrhosis .
Skeletal and cardiac muscle involvement also varies widely, with reports of asymptomatic cardiomyopathy, symptomatic cardiomyopathy leading to death, ventricular hypertrophy, sudden death due to cardiac arrhythmia, and slowly progressing myopathy with distal, proximal or generalized myopathy.

Currently, there is no approved treatment for GSD III, and symptoms are managed with nutrition intervention, including small, frequent feedings and cornstarch to avoid hypoglycemia in children, a high protein diet, low complex carbohydrates, avoidance of fasting, and avoidance of simple sugars. Current nutrition management is focused on prevention of hypoglycemia and maintenance of glucose levels. Case reports indicate that a strict ketogenic regimen may reduce hypertrophic cardiomyopathy .
No specific management approach has been shown to address the progressive and debilitating muscle impairment experienced by patients with GSD III. The current treatment approach of nutrition management is supportive, but incomplete, and highlights a need for a targeted therapy that replaces the missing or defective enzyme.

Study objective

The primary objective of this study is to evaluate the incidence of hypoglycemia in adult and pediatric patients with GSD III.

The secondary objective of this study is to evaluate the sensitivity of various muscle strength and function measures to detect deficits in patients with Glycogen Storage Disease (GSD) III.

Study design

This is a non-interventional clinical survey study in patients >= 1 year of age with GSD III

Study burden and risks

No investigational product (IP) or reference product will be administered as part of this study.
The burden associated with participation in this study is the time taken to complete study assessments, the travel taken for any onsite visits, and potential for mild discomfort from participating in procedures and assessments, including discomfort and local skin irritation from
the continuous glucose monitor (CGM) and finger sticks for handheld glucometer (HHG).
Patients may directly benefit by having previously undetected disease manifestations, including asymptomatic hypoglycemia, identified during the

study assessments. This may lead to improved dietary management.
With no treatments currently available for this disorder, a clear medical need exists for a novel therapeutic that could alter the clinical course of the disease. This study is being conducted to support the clinical development of a novel therapy for GSD III. In participating, subjects may indirectly benefit by contributing to the understanding of GSD III and the development of new therapies.

Contacts

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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)
Babies and toddlers (28 days-23 months)

Inclusion criteria

1. Male or female 1 year of age or older at time of informed consent/assent
2. Diagnosis of GSD III, confirmed by AGL sequencing or GDE enzymatic testing
3. Provide informed consent after the nature of the study has been explained, and prior to
any research-related procedures. If a minor or an adult with cognitive limitations, willing
and able (if possible) to provide assent and have a legally authorized representative
provide informed consent after the nature of the study has been explained, and prior to
any research-related procedures

Exclusion criteria

1. Subject is unwilling to remain blinded to CGM data, or the Investigator determines that blinding would compromise subject safety
2. Presence or history of any condition that, in the view of the Investigator, would interfere with participation or pose undue risk
3. Use of any IP or investigational medical device within 30 days or 5.5 half-lives, whichever is longer, prior to screening, or during the study

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2022
Enrollment:	2
Type:	Actual

Ethics review

Approved WMO Date:	10-08-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL80008.042.22

Study results

Results posted: 12-03-2024

First publication
23-01-2024