A Long-Term Follow-up Study to Evaluate the Safety and Efficacy of Adeno-Associated Virus (AAV) Serotype 8 (AAV8)-Mediated Gene Transfer of Glucose-6-Phosphatase (G6Pase) in Adults with Glycogen Storage Disease Type Ia (GSDIa)

Published: 18-05-2021
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This study has been transitioned to CTIS with ID 2023-504004-29-00 check the CTIS register for the current data. To determine the long-term safety of DTX401 following a single IV dose in adults with GSDIa

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

Summary

ID

NL-OMON54186

Source
ToetsingOnline

Brief title
401GSDIA02

Condition

- Metabolic and nutritional disorders congenital

Synonym
GSDIa, Von Gierke Disease

Research involving
Human

Sponsors and support

Primary sponsor: Ultragenyx Pharmaceutical Inc
Source(s) of monetary or material Support: Ultragenyx Pharmaceutical Inc.

Intervention

Keyword: Adeno-Associated Virus Serotype 8, Glucose-6-Phosphatase (G6Pase), Glycogen Storage Disease Type Ia (GSDIa)

Outcome measures

Primary outcome

Primary objective: to determine the long-term safety of DTX401 following a

single IV dose in adults with GSDIa

Primary endpoint: the incidence of AEs and SAEs for each dose level assessed by

severity and

relationship to IP

Secondary outcome

Secundary objective: to evaluate the long-term effect of DTX401 on symptom-free

euglycemia in a setting

of a controlled fasting challenge

Secundary endpoint: the change from Day 0 (Study 401GSDIA01) in time to first

hypoglycemic event during a controlled fasting challenge over time by cohort,

following IV administration of DTX401

Study description

Background summary

Study 401GSDIA02 is a long-term follow-up study to evaluate the safety and efficacy of adeno-associated virus (AAV) serotype 8 (AAV8)-mediated gene transfer of glucose-6-phosphatase (G6Pase) in adults with glycogen storage disease type Ia (GSDIa). Only subjects who received DTX401 in Study 401GSDIA01 are eligible to participate in Study 401GSDIA02. Study 401GSDIA01 was a Phase 1/2, open-label safety and dose-finding study of AAV8-mediated gene transfer of G6Pase in adults with GSDIa, during which subjects received a single intravenous (IV) dose of DTX401. No investigational product will be administered during Study 401GSDIA02.

GSDIa is an inherited disorder caused by a deficiency in the gene (referred to as G6PC) for glucose-6-phosphatase (G6Pase). Because of this deficiency, people with GSDIa are not able to maintain safe and healthy levels of blood sugar (glucose).

People with GSDIa develop low blood sugar (hypoglycemia) within a few hours after eating unless they manage their blood sugar with cornstarch or other dietary therapy. If low blood sugar levels are not treated properly, serious side effects, such as seizures or even death, can occur. GSDIa can also prevent some of the body*s organs and tissues from working normally.

The DTX401 vector is called adeno-associated virus (AAV); it is used to deliver the G6PC gene to your liver. AAV is a common virus found throughout the body in natural infections. It is not currently known to cause disease.

Study objective

This study has been transitioned to CTIS with ID 2023-504004-29-00 check the CTIS register for the current data.

To determine the long-term safety of DTX401 following a single IV dose in adults with GSDIa

Study design

In Study 401GSDIA02, subjects will be followed for approximately 4 years, for a total of 5 years of follow-up after administration of DTX401 in Study 401GSDIA01. Subjects will visit the study site approximately every 13 weeks during the first year of Study 401GSDIA02 and then approximately every 26 weeks through the end of the study at Week 260 (Year 5) for safety and efficacy evaluations. Subjects who are waiting to enroll in the DTX401 disease monitoring program [DMP] at the end of Year 5 may continue for up to 1 additional year in the study, thus having a follow-up until Week 312 (i.e. total follow-up of approximately 6 years after the administration of DTX401). Once the DMP is available to enroll, subjects can enter the DMP after the Study 401GSDIA02 Week 208 visit has been completed. The DMP is a long-term follow-up

study to evaluate safety and effectiveness of DTX401 for at least 10 years after DTX401 administration. The DMP for GSDIa will be conducted under a separate protocol.

Study burden and risks

Please refer for an overview of study procedures to table 1, in the protocol.

Subjects mainly have to follow the following study procedures:
* medical history and physical exam
* carrying continuous glucose monitoring device (CGM)
* completing questionnaires
* urine and blood sampling
During the inpatient days also:
* ECG, ultrasound liver, MRI liver
* controlled fasting challenge
* 24h urine sample collection
* 30 min telephone interview

During this study, there are no IP associated risks, since no IP will be provided. Potential risks for the patient are associated with the various study procedures, such as ECG (e.g. skin irritation), blood sampling (e.g. potential painful site needle puncture), controlled fasting challenge (e.g. sweating, confusion) etc.

Below you can find the explained risks for subjects:
Potential Risks Associated with Study Procedures
You will be asked to give several blood samples during the study. Over the course of the study, you will give about 1250 mL of blood in total.

You may experience pain, a pinching feeling, or bruising at the site where the needle is inserted. There is a small risk of infection at the needle puncture site. Some people experience dizziness, upset stomach, or fainting when their blood is drawn. Blood will be drawn by a qualified person who will ensure that all safety measures are followed to reduce the risks. The intended use of the blood samples is to assess and monitor your safety to participate in the study. If an important change is observed, the study doctor will review the results and will provide proper care.

You will be asked to undergo an ultrasound of your liver during specific study visits. There are no significant risks due to ultrasound. You may feel uncomfortable when the gel is applied and while the technician is pressing the hand-held device on your body to locate your liver.

You will be asked to undergo MRI scans periodically during the study. There are no significant risks due to MRI scans. You may be bothered by the sounds made by the MRI machine and by feelings of being closed in (claustrophobia). In some

rare cases, nausea and dizziness have been reported. There is a risk of distress due to the closed space of the scanner. However, you will be provided with a panic button which, when pressed, will alert the technician to stop the test. Because the MRI involves use of a large magnet, there may be risks if you have metal in your body that you have not disclosed to the study staff. Before the MRI scan is performed, be sure to tell the study staff if you have any of the following:
• Pacemaker
• Heart or vascular clip (including an aneurysm clip)
• Prosthetic heart valve
• Metal prosthesis (for example, an artificial hip or knee joint)
• Pregnancy
• Distress due to closed space
• Metal fragments in body
• Transdermal patches (Patches must be removed before the MRI scan. You may bring another patch to reapply after your scan.)
• Color contact lens
• Body piercing
• Permanent make up or tattoo

Potential Risks Associated with COVID-19
Depending on the current status of the COVID-19 pandemic, the study doctor may make adjustments to your visit schedule or change the type of visit you have. If your visit is changed to a remote visit, the visit-specific assessments may be collected by a home health nurse to protect your health and well-being.

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

1. Received DTX401 in Study 401GSDIA01.
2. Willing and able to provide written informed consent after the nature of the study has been explained, and prior to any research-related procedures being performed.
3. Willing and able to comply with all scheduled study visits, procedures, and requirements.

Exclusion criteria

1. Planned or current participation in any other interventional clinical study that may confound the safety or efficacy evaluation of DTX401 during this study.
2. Presence or history of any condition that, in the view of the Investigator, poses a risk to subject safety or places the subject at high risk of poor compliance or not completing the study or that would significantly affect the interpretation of study results.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-10-2021
Enrollment:	2
Type:	Actual

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-08-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-02-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-02-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	28-06-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-09-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	CTIS2023-504004-29-00
EudraCT	EUCTR2018-004473-27-NL
ClinicalTrials.gov	NCT03970278
CCMO	NL77529.000.21