These Clinical Study Results are provided for informational purposes only.

This lay summary is a brief summary of the main results from a clinical study. The study listed may include approved and non-approved uses, formulations or treatment regimens. It is not intended to promote any product or indication and is not intended to replace the advice of a healthcare professional. The results reported in any single clinical trial may not reflect the results obtained across the full clinical development program. Only a physician can determine if a specific product is the appropriate treatment for a particular patient. If you have questions, please consult a health care professional. Before prescribing any product, healthcare professionals should consult the regional approved product labeling for indications and proper use of the product.

Clinical Study Results

A Study of DTX401 in Children and Adults With Glycogen Storage Disease Type Ia (GSDIa)

Thank you!

Thank you to the participants and caregivers who took part in the clinical study, **DTX401-CL301**. Ultragenyx, the sponsor of this study, is grateful and believes it is important to share the results with the participants and their families.

By taking part in this study, the participants helped researchers learn more about using **DTX401** in people with **GSDIa**.

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Why was this study needed?

Researchers designed this Phase 3 study, **DTX401-CL301**, to understand how well DTX401 worked and to learn more about its safety in adults and children aged 8 years or older with **GSDIa**. Phase 3 studies look to see how well a new drug works compared to current standard treatment or placebo in larger groups of people.

What is GSDIa?

GSDIa is a rare, **genetic condition** that prevents the body from keeping blood sugar levels normal between meals. This leads to low blood sugar (hypoglycemia) that can be life-threatening.

A **genetic condition** is passed on from parent to child through genes that do not work properly. Genes are small pieces of DNA that provide instructions for making proteins that are needed for your body to grow and work.

What causes GSDIa?

GSDIa is caused by changes (known as variants) in the gene *G6PC*, which makes an enzyme called G6Pase. G6Pase is needed to make and release glucose into the blood. In people with **GSDIa**, changes in *G6PC* lead to a missing or nonworking type of G6Pase. This can lead to a build up of glycogen and other substances that can damage certain organs, like the liver and kidneys.

Currently, people with **GSDIa** manage their symptoms by closely watching their physical activity and blood sugar levels, following a special meal plan, avoiding certain types of sugar, and taking cornstarch by mouth between meals. Cornstarch is a type of carbohydrate that is broken down into glucose over a longer period of time. The slow release of glucose can help keep blood sugar levels from dropping to dangerously low between meals.

How does the body usually keep blood sugar levels normal?

When the body does not need to use blood sugar **(glucose)** for energy right away, it stores it as **glycogen** in the muscles and liver.

When the body needs energy between meals, the enzyme called **G6Pase** turns glycogen back into glucose for the body to use as energy and keep blood sugar levels normal. An **enzyme** is a special type of protein in the body that helps chemical reactions happen faster.

What is DTX401?

DTX401, also called pariglasgene brecaparvovec, is an AAV8-based **gene therapy** designed as a one-time dose to treat GSDIa by adding a working copy of *G6PC* gene to make a working G6Pase. The treatment is given one time, through a vein as an intravenous (IV) infusion.

A **gene therapy** is a type of treatment that is designed to change a disease-causing gene or add a working copy of a gene to help the body function better.

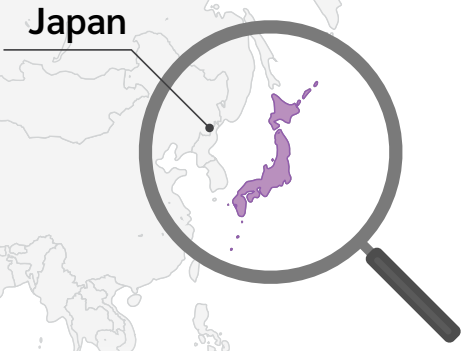
Who was in this study?

This study included **46 participants** with **GSDIa** from Brazil, Canada, Denmark, Germany, Italy, the Netherlands, Spain, and the United States.

The participants included **27 males and 19 females** between **8 to 37 years old** when they joined the study. The average age was 21 years old.

There was also a separate part of this study done in **Japan**. This was done so that Japan could have access to DTX401 in a similar timeframe as other parts of the world. In Japan, **3 participants** with **GSDIa** were treated with DTX401.

All **3 participants** in the **Japan group** were **males** between **11 to 17 years old**. The average age was 13 years old.



What happened during this study?

The study started in **November 2021** and the last participant visit was in **February 2026**. Participants were in the study for about 1 to 3 years.

Screening Period

- The researchers checked each participant's health to make sure they could join the study. This period lasted up to 16 weeks to ensure cornstarch, diet, and glucose control were stable.
- Participants had to show 4 continuous weeks of stable blood sugar, diet, and cornstarch intake before they could receive treatment.

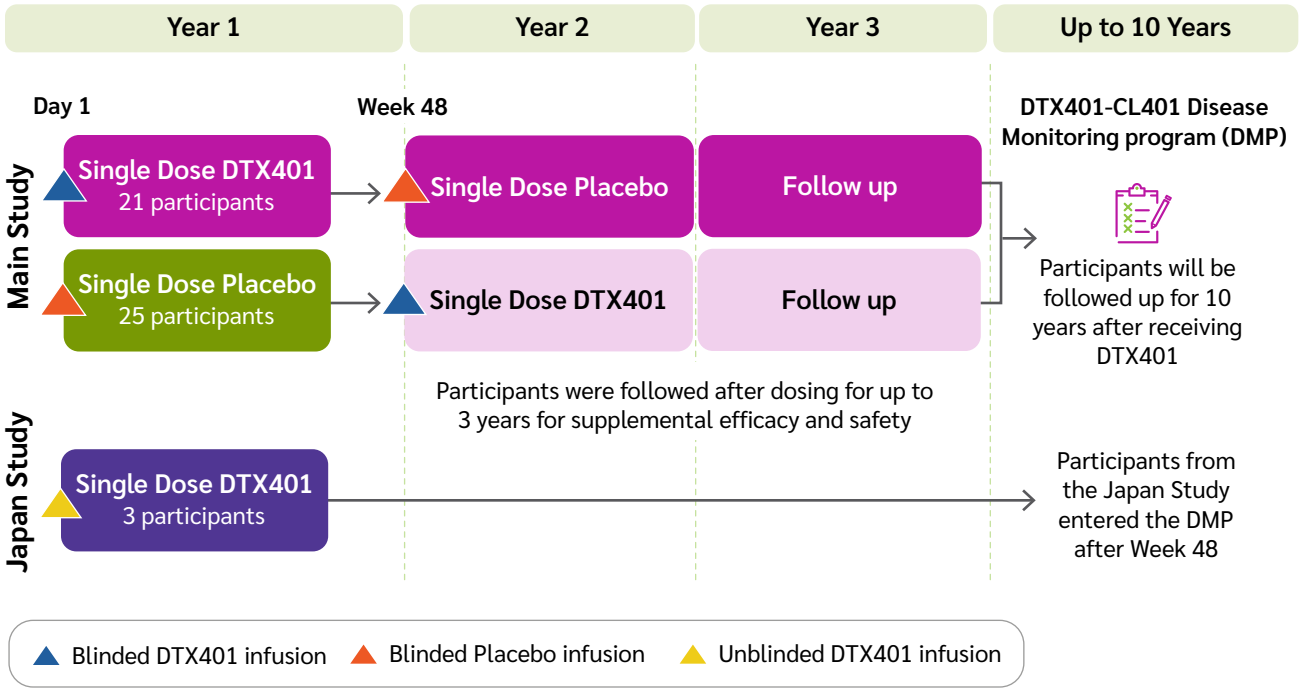
Treatment Period

- The main study was blinded so participants did not know what they received at Week 1 and at Week 48. The study in Japan was not blinded, and these participants did not receive placebo.
- On Day 1, participants in the main study were randomly assigned to receive a single dose of DTX401 or placebo. In the Japan study, all participants received DTX401.
    - A placebo looks like and is delivered in the same way as the study drug but does not contain any medicine in it. This helps researchers understand the real effects of the medicine.
- At Week 48, participants who had received DTX401 at the start of the main study received placebo and those who had received placebo received DTX401. The Japan study ended at Week 48.
- The DTX401 dose was measured in **genome copies (GC)**, which are tiny units of the medicine, per kilogram of body weight (GC/kg). Participants received $1x10^{13}$ GC/kg of DTX401.
- 15 days after dosing, participants who received DTX401 also received a steroid (prednisolone) to reduce the possible side effects on the liver. Participants who received placebo were given a placebo version of the steroid.

Follow-up Period

- Participants from the main study were followed for another 2 years after Week 48. Participants from the Japan study ended the study at Week 48. At the end of the study, all participants were invited to join the DTX401-CL401 **Disease Monitoring Program (DMP)**.
- A **DMP** is a study that collects data from a larger group of participants over a long period of time. The data from a DMP helps researchers and people better understand the disease, how treatments work over time, and how treatments work in real life outside of clinical study activities.

The graphic below shows how the study was done.



What did researchers learn from this study?

This is a **summary** of the key results from this study. Each participant's individual results might be different. If you took part in this study and have questions about this results summary, please contact the study site.

The results from several studies are needed to decide if treatments are safe and work to treat a condition. Other studies may give new information or different results. Always talk to a doctor before making any treatment changes.

This study was designed to answer the **main question:**

- **Could DTX401 reduce the amount of cornstarch participants used over a 24-hour period?**

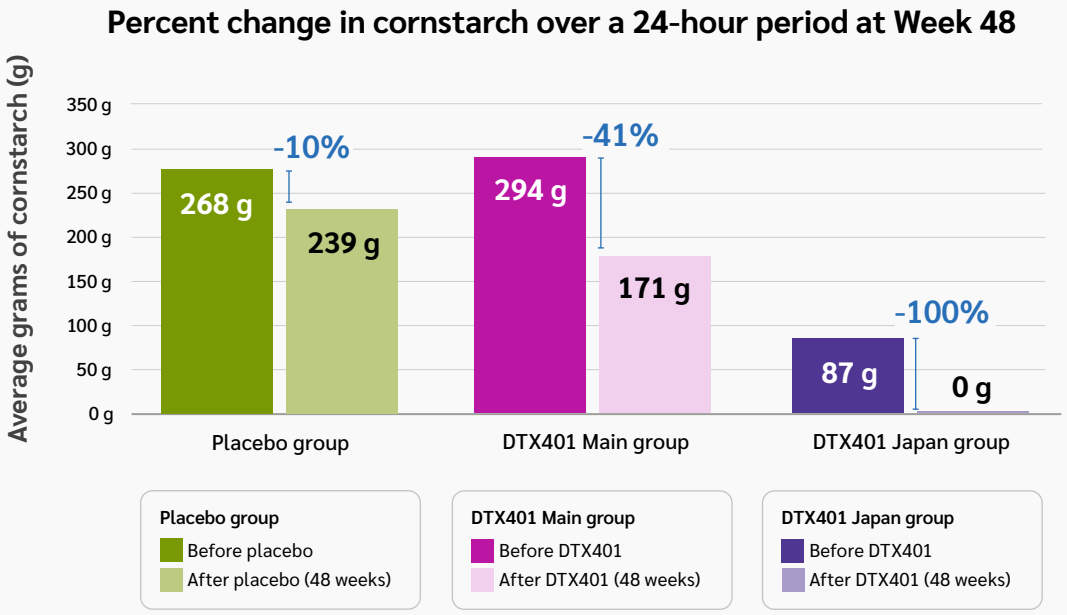
Other questions that the researchers wanted to answer in addition to the main question:

- Was there a change in the number of doses of cornstarch used over a 24-hour period?
- Was there a change in participants' blood sugar levels?
- Could participants go for longer between meals before getting low blood sugar?
- Did participants notice changes in GSDIa symptoms?
- How many participants had medical problems, called **adverse events** during the study?
- What **possible side effects** happened during the study?

Could DTX401 reduce the amount of cornstarch participants used over a 24-hour period?

Overall, researchers found that, 48 weeks after treatment, there was a change in the participants' cornstarch use.

To answer this question, participants reported the amount of cornstarch (in grams) they used over a 24-hour period. The graph below shows the change in daily cornstarch use over a 24-hour period.

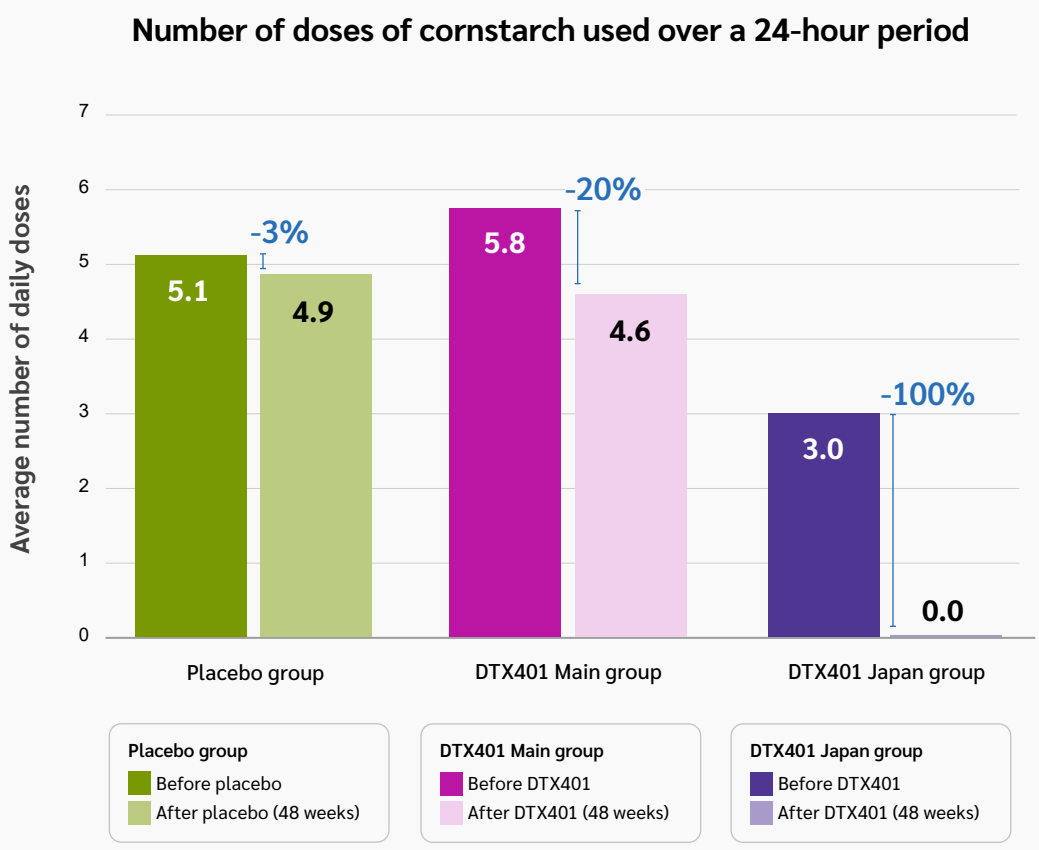


The remaining results were not the main questions the study wanted to answer. Researchers believed the following results would be interesting to people with GSDIa.

Was there a change in the number of doses of cornstarch used over a 24-hour period?

Overall, the average number of reported cornstarch doses over a 24-hour period changed after receiving treatment.

The graph below shows the number of doses of cornstarch used over a 24-hour period.

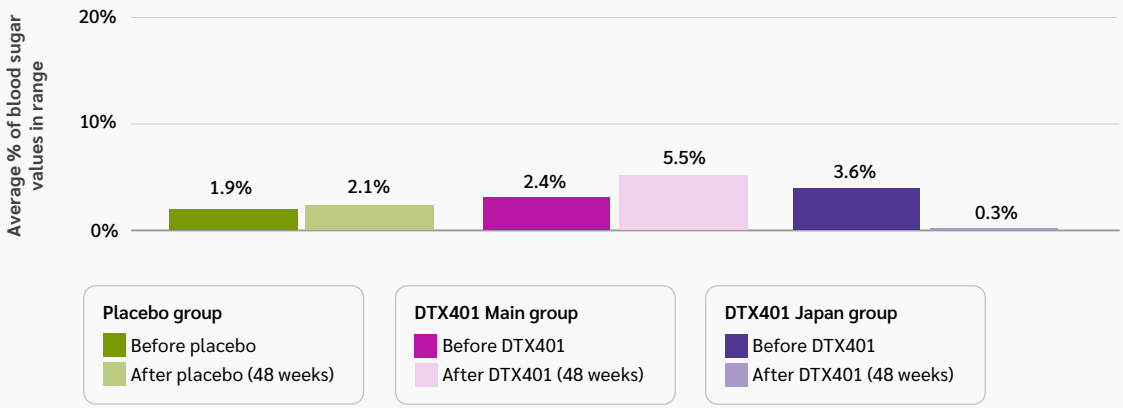


Was there a change in participants' blood sugar levels?

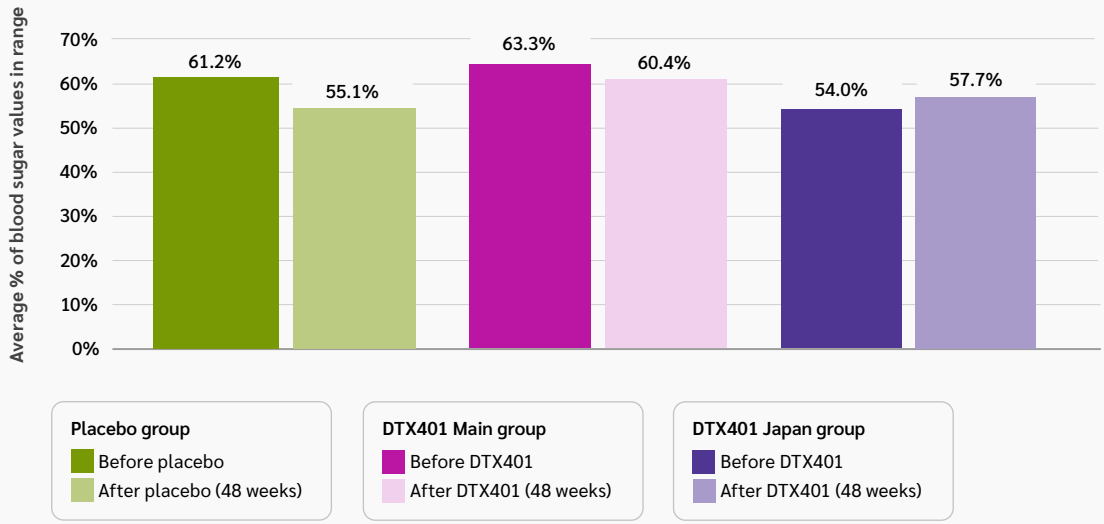
The study looked at whether the treatment worked at least as well as placebo in avoiding low sugar levels. They found that the placebo group and treatment groups maintained similar blood sugar levels below 70 milligrams of sugar per deciliter of blood (mg/dL).

The graphs below show participants' blood sugar levels in different ranges.

Percent of blood sugar values below 70 mg/dL



Percent of blood sugar values between 70-120 mg/dL



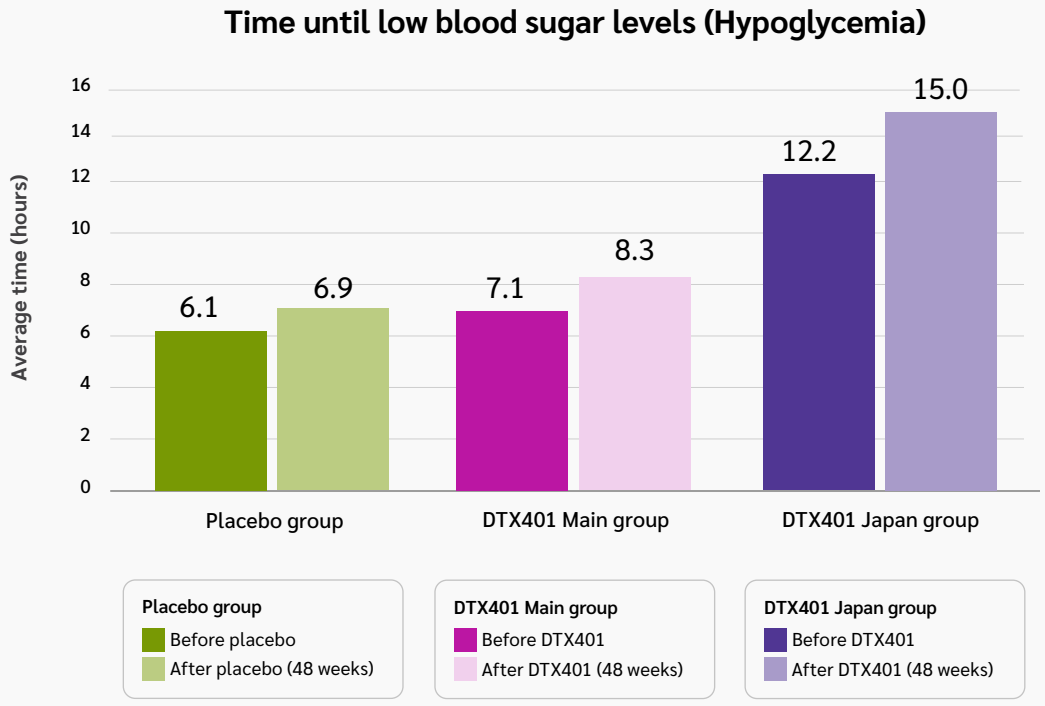
Could participants go for longer between meals before getting low blood sugar?

Researchers learned about the time participants could fast (not eat or drink anything but water) before getting low blood sugar by doing a **controlled fasting challenge**.

What is a controlled fasting challenge?

Participants stayed in the hospital overnight. They received dinner and later their standard evening dose of cornstarch. After that, they did not eat or drink anything but water. The researchers tested their blood sugar levels many times until the participant had a low blood sugar or showed symptoms of low blood sugar, or reached 15 hours of fasting. Low blood sugar was defined as 54 mg/dL or lower.

The graph below shows the average number of hours from after participants' dinner until low blood sugar occurred.



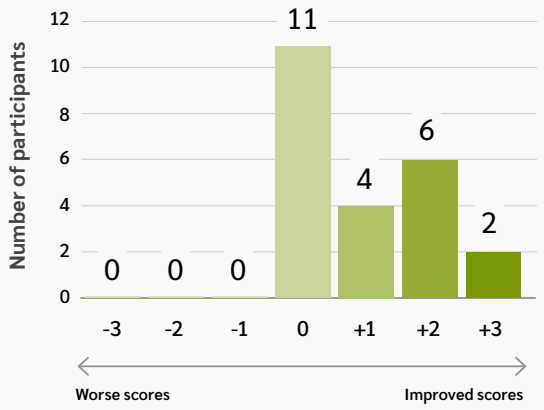
Did participants notice changes in GSDIa symptoms?

Researchers answered this question by having participants complete the **Patient Global Impression of Change (PGIC)** questionnaire.

The PGIC is a questionnaire that asks participants to rate how much their GSDIa symptoms changed since they started the study. Participants must select one response from the following list of options: Much worse (-3), Moderately worse (-2), Minimally worse (-1), No change (0), Minimally improved (+1), Moderately improved (+2), Much improved (+3). Scores range from -3 to +3, and higher scores mean improved GSDIa.

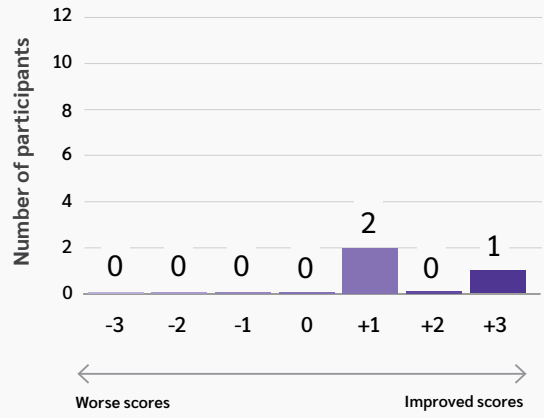
The graph below shows the PGIC scores of participants at Week 48.

PGIC scores at Week 48 (Placebo group)



PGIC scores at Week 48 (DTX401 Main group)

PGIC scores at Week 48 (DTX401 Japan group)



How many participants had medical problems, also called adverse events, during the study?

During the first 48 weeks of the study, 46 of 49 participants had at least 1 adverse event and 11 of 49 participants had serious adverse events.

Of the participants who continued beyond Week 48, 40 of 40 had a total of at least 1 adverse event and 21 of 40 participants had serious adverse events.

No participants died during the study.

What is an adverse event?

An **adverse event** is an unwanted or unexpected sign or symptom that happens after taking the study treatment.

A lot of research is needed to know if a treatment causes an adverse event. Adverse events **may or may not be caused by the study treatment**, other drugs taken while in the study, the participants' medical history, or procedures performed in the study.

What is a serious adverse event?

An adverse event is considered **serious** when it:

- Is considered medically important by a doctor
- Requires hospitalization
- Causes a disability or birth defect
- Is life-threatening
- Causes death

This section is a summary of all adverse events that happened during the study, even if the doctors thought they might not be caused by the study treatment.

The tables below show the number of participants who had adverse events during the study.

Number of participants who had at least 1 event through Week 48:

	Placebo group	DTX401 Main group	DTX401 Japan group
Adverse event, including serious adverse events	22 out of 25 participants **(88%)**	21 out of 21 participants **(100%)**	3 out of 3 participants **(100%)**
Serious adverse event	3 out of 25 participants **(12%)**	8 out of 21 participants **(38%)**	0 out of 3 participants **(0%)**

Number of participants who had at least 1 event through Week 144:

	All main study participants who received DTX401
Adverse event, including serious and other adverse events	40 out of 40 participants **(100%)**
Serious adverse event	21 out of 40 participants **(53%)**

This section is a summary of the **possible side effects**.

What's the difference between a possible side effect and an adverse event?

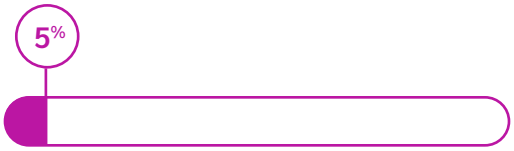
A **possible side effect** is an adverse event that the doctors thought **might be caused by the study treatment or study procedure.**

Not all adverse events are side effects.

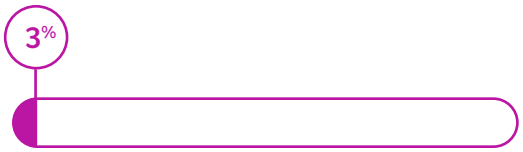
During this study, 32 of 40 participants (80%) from the main study had possible side effects, and all 3 participants (100%) in the Japan group had possible side effects.

What serious possible side effects did participants have during this study?

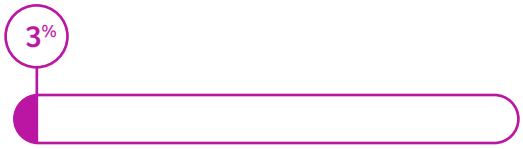
During this full study, 4 participants had serious possible side effects. The serious side effects were:



Severe allergic reaction during the infusion
(Anaphylactic reaction or Infusion-related reaction)
2 of 40 participants



High lactic acid levels in the blood
(Hyperlactacidaemia)
1 of 40 participants



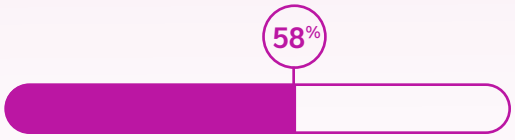
High triglyceride level in the blood
(Hypertriglyceridemia)
1 of 40 participants

None of the participants from the Japan group had serious possible side effects.

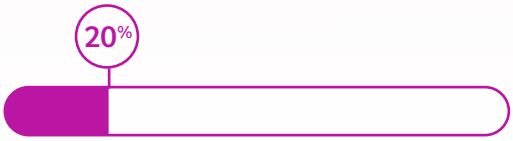
What other possible side effects did participants have during the study?

Other possible side effects were those that did not meet the criteria to be considered as "serious". The other common possible side effects that happened were **certain types of increased liver enzymes**, as shown below.

DTX401 Main group

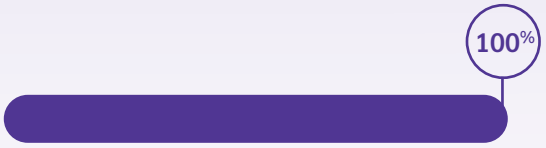


Transaminases increased
23 of 40 participants

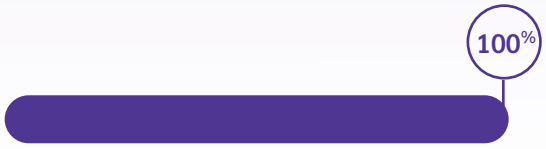


Alanine aminotransferase increased
8 of 40 participants

DTX401 Japan group



Alanine aminotransferase increased
3 of 3 participants



Aspartate aminotransferase increased
3 of 3 participants

Only the most common side effects are listed above. Any other side effects were reported by fewer than 8 participants in the main study and fewer than 2 participants in the Japan study. There were other possible side effects that happened in fewer participants.

How has this study helped participants and researchers?

- During this study, researchers found that after treatment with DTX401, participants could use less cornstarch and use it less frequently. They also found that participants on treatment experienced similar glucose levels to those on placebo and that they saw changes in their GSDIa symptoms.
- Researchers also found the most common side effects thought to be related to DTX401 treatment were certain types of increased liver enzymes. No new or unexpected safety concerns were observed during the study.

Ultragenyx has ongoing studies of DTX401 in participants with **GSDIa**.

Other studies may have new or different results. Always talk to a doctor before making any treatment changes.

Where can I learn more about this study?

You can find more information about this study, including a report with the study's results, on these websites:

- https://clinicaltrials.gov/ct2/show/NCT05139316
- https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2023-508750-25-00

Official Study Title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Adeno-associated Virus Serotype 8-mediated Gene Transfer of Glucose-6-phosphatase in Patients With Glycogen Storage Disease Type Ia

National Clinical Trial number: NCT05139316

EU CT number: 2023-508750-25-00

If you have questions about the results, please speak with a doctor or staff at the study site.

Thank you!

At Ultragenyx, our focus is developing medicines for people who live with rare and ultra-rare diseases. But it takes more than scientific knowledge and research to develop medicines. Your involvement is essential and ensures that the research process moves forward. Thank you for your participation in this study and commitment to research.

Ultragenyx is a biopharmaceutical company committed to bringing to patients products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases.

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