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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 health care 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 to learn about the safety of UX053 in patients with glycogen storage disease type III (GSD III)

Thank you!

Thank you to the patients who took part in the clinical study for UX053. Ultragenyx, the sponsor of this study, is grateful to those who participated and believes it is important to share the results with the patients.

By taking part in this study, the patients helped the researchers learn more about using UX053 in people with GSD III.

Contents

Why was this study needed?

Researchers designed this study, **UX053-CL101**, to learn about the safety of different doses of UX053 in patients with any subtype of glycogen storage disease type III (GSD III). Researchers also wanted to learn how long different doses of UX053 stayed in the blood. The study was not designed to learn if UX053 is effective (works) to treat GSD III.

This study was the first time that UX053 was given to people.

GSD III is a rare, genetic condition that causes liver damage and prevents the body from maintaining normal blood sugar levels between meals. It can also cause damage to the muscles and heart.

GSD III is caused by changes (variants) in the gene *AGL*, which makes a protein called glycogen debranching enzyme (GDE). GDE helps fully breakdown glycogen into glucose. In people with GSD III, *AGL* makes a nonworking GDE that cannot fully break down glycogen into glucose. Partially broken-down glycogen can build up and damage the muscles, heart, and liver.

There is no approved medicine for GSD III. Currently, people with GSD III manage their symptoms by following a special high protein meal plan, avoiding certain types of sugar, and taking cornstarch.

How does the body usually keep normal blood sugar levels?

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

When the body needs energy between meals, proteins, including GDE, turn glycogen back into glucose to use as energy and keep normal blood sugar levels.

What is UX053?

UX053 is an mRNA therapy designed to treat GSD III by giving the body mRNA with instructions to make a working GDE in the liver. UX053 is made of mRNA and fatty particles that may protect the mRNA and carry it into liver cells. As a possible treatment, UX053 is designed to be given many times. In this study, patients received UX053 only one time through a needle in a vein as one intravenous (IV) infusion.

What is mRNA and mRNA therapy?

Messenger RNA (mRNA) is inside of all cells in the body and carries the instructions that tell cells to make a protein. **mRNA therapy** gives the body mRNA with instructions to make a working protein. This type of treatment does not change the genes stored inside the cells. A patient must continue to receive doses of mRNA therapy over time to keep making the working protein.

Who was in this study?

This study included **8 patients** with any subtype of GSD III from these countries:

- Italy
- Spain
- United States

The patients included men and women between 36 to 58 years old when they joined the study. Their average age was 48 years old.

What happened during this study?

Before treatment

The study doctors checked each patient's health to make sure they could join the study.

During treatment

Each patient received one dose of UX053 through one IV infusion that lasted at least 4 hours. Patients were assigned to one of these groups:

- **Group 1** received a **lower dose** of UX053
- **Group 2** received a **higher dose** of UX053

All patients were also given other medicines to take by mouth an hour before receiving UX053. The other medicines were to prevent the immune system from overreacting, which is called an immune reaction.

More groups and doses were planned, but did not start because the study ended early.

After treatment

After the patients received UX053, staff took blood samples for 1 month and checked their health for about 3 months.

The study started in October 2021 and ended early in March 2023. Each patient was in the study for about 3 months.

Ultragenyx completed the first part of this study, which was to learn about patients receiving one dose of UX053. Ultragenyx made the difficult decision to end the study early to focus limited resources on later phase studies. This decision was not due to any concerns about the safety of UX053 or its effects on GSD III.

What did researchers learn from this study?

This is a **summary** of the main results from this study. Each patient's individual results might be different and are not shown in this summary. If you took part in this study and have questions about your results, please contact the study site.

The results from several studies are needed to decide if treatments are safe and work. 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 question:**

- **How safe is UX053 in treating patients with GSD III?**

To answer this question, researchers looked at:

- How many patients had medical problems called adverse events during the study
- What side effects happened during the study - a side effect is an adverse event that doctors thought might be caused by the study treatment

This study was also designed to answer the question:

- How long did different doses of UX053 stay in the blood?

How many patients had medical problems called adverse events during the study?

7 of the 8 patients had adverse events, none of which were considered serious.

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 patients' 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 table below shows the number of patients who had adverse events during the study.

Number of patients who	**Group 1** Lower dose of UX053	**Group 2** Higher dose of UX053
Had any adverse event	**3 of 4 patients** (75%)	**4 of 4 patients** (100%)

There were no serious adverse events during this study.

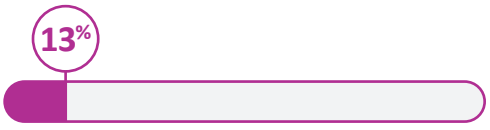
The next section is a summary of the side effects.

What's the difference between a side effect and an adverse event?
A **side effect** is an adverse event that the doctors thought **might be caused by the study treatment.** Not all adverse events are side effects.

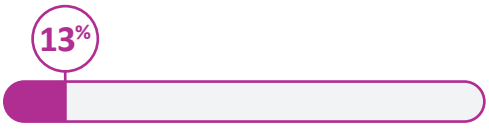
What side effects happened during the study?

One patient in Group 2 had side effects, which were low blood sugar and back pain that happened during the infusion. These side effects were not serious and went away within a few hours. No patients in Group 1 had side effects. No patients had serious side effects thought to be caused by the study treatment.

Below are the side effects that the doctors thought might be caused by the study treatment.



Low blood sugar
(hypoglycemia)
1 of 8 patients



Back pain
1 of 8 patients

How long did different doses of UX053 stay in the blood?

Overall, different doses of UX053 stayed in the blood for about 2 to 3 weeks after patients received UX053. There was a trend of the higher dose of UX053 reaching higher levels in the blood than the lower dose.

To answer this question, researchers took blood samples from each patient up to 1 month after they received UX053. The researchers measured the level of UX053 mRNA and fatty particles in the blood samples to better understand how long UX053 stays in the blood. More research is still needed to know the dose that may have an effect on GSD III.

How has this study helped patients and researchers?

Overall, the researchers learned about the safety of UX053 and concluded that single infusions of UX053 were generally well-tolerated.

The researchers also found that different doses of UX053 stayed in the blood for about 2 to 3 weeks after patients received UX053.

Ultragenyx is considering ways to support future studies in GSD III. When this summary was written, Ultragenyx did not have a timeline for future studies of UX053 in patients with GSD III.

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/study/NCT04990388
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2021-000903-19/ES

Official Study Title: A phase 1/2 first-in-human, study to evaluate the safety, tolerability, and pharmacokinetics of single ascending doses and repeat doses of UX053 in patients with GSD III

National Clinical Trial number: NCT04990388

EudraCT number: 2021-000903-19

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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