

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 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 summary of findings of DTX101 in patients with Hemophilia B

Thank you!

Thank you to the patients, and their caregivers, who took part in the clinical studies for AAVrh10FIX, also called DTX101. Ultragenyx, the sponsor of these studies, is grateful to those who participated and believes it is important to share the results.

By taking part in these studies, the patients helped the researchers learn more about using DTX101 in people with Hemophilia B, also called HemB.

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Why were the studies needed?

Researchers designed the **101HEMBO1** study to learn what dose of DTX101 works best in patients with HemB. The **101HEMBO2** study was designed to follow these patients to learn more about the long-term safety of DTX101 and to learn if DTX101 helped patients with HemB.

Hemophilia B, or **HemB**, is a rare genetic bleeding disorder. In patients with HemB, a protein called factor IX, or FIX, does not work properly. FIX normally helps blood clot after an injury. This means that when patients with HemB get an injury or cut, their blood does not clot as well and it is harder for them to stop the bleeding.

HemB can cause serious health problems, such as frequent, sudden internal bleeding, which can lead to:



Chronic Arthropathy

Pain and swelling in the joints that does not go away



Intracranial Hemorrhage

Bleeding inside of the skull, which can cause pressure to build up on the brain

What is DTX101?

DTX101, also known as AAVrh10FIX, is a type of study treatment called “**gene therapy.**” DTX101 is designed to work by adding a working copy of the FIX gene into the cells of patients with HemB. Adding a functioning copy of the gene could help patients make the FIX protein necessary for blood clotting.

Who was in the studies?

- The 101HEMB01 and 101HEMB02 studies included 6 male patients with moderate/severe or severe HemB
- Patients joined these studies from the United States and the United Kingdom
- Patients were 28 to 70 years old at the start of the first study (101HEMB01)
- After completing the 101HEMB01 study, all patients participated in the 101HEMB02 study
- During the 101HEMB01 study, patients received a single treatment with one of two doses of DTX101 by intravenous infusion, which is a slow injection of the medicine into a vein in the arm. Doses were based on the amount of DTX101, called genome copies or GC, per kilogram of each participant’s body weight, also called GC/kg.

The two dose groups were:



Group 1:
3 patients received a low dose (1.6×10^{12} GC/kg) of DTX101



Group 2:
3 patients received a higher dose (5.0×10^{12} GC/kg) of DTX101

No DTX101 was given during the 101HEMB02 follow-up study.

What happened during the studies?



Before treatment

The study doctors checked each patient's health and medical records to make sure they could join the study. For example, the doctors made sure participants did not currently or previously have liver disease, hepatitis, or certain viral infections.



During treatment with DTX101

At the start of the **101HEMBO1** study, each patient received a single slow injection of DTX101 into a vein in the arm, called an infusion, during a clinic visit. In some cases, patients may also have received FIX (e.g., ALPROLIX®) infusions to treat frequent bleeding episodes.



After treatment

After treatment in the **101HEMBO1** study, patients were seen by the study doctors every 2-4 weeks to check on their health. After approximately 1 year, patients could participate in the **101HEMBO2** study where they were seen by the study doctors approximately once a year to check on their health for at least 4 additional years.

The **101HEMBO1** study started in December 2015 and ended in October 2017.

The **101HEMBO2** study started in January 2017 and ended in December 2021.

What were the results from the studies?

This is a **summary** of the main results from the studies. 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 doctor or staff at the study site.

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

The 101HEMB01 and 101HEMB02 studies were designed to answer **2 main questions**:

- Did either dose of DTX101 help patients make the FIX protein?
- What side effects happened during these studies?

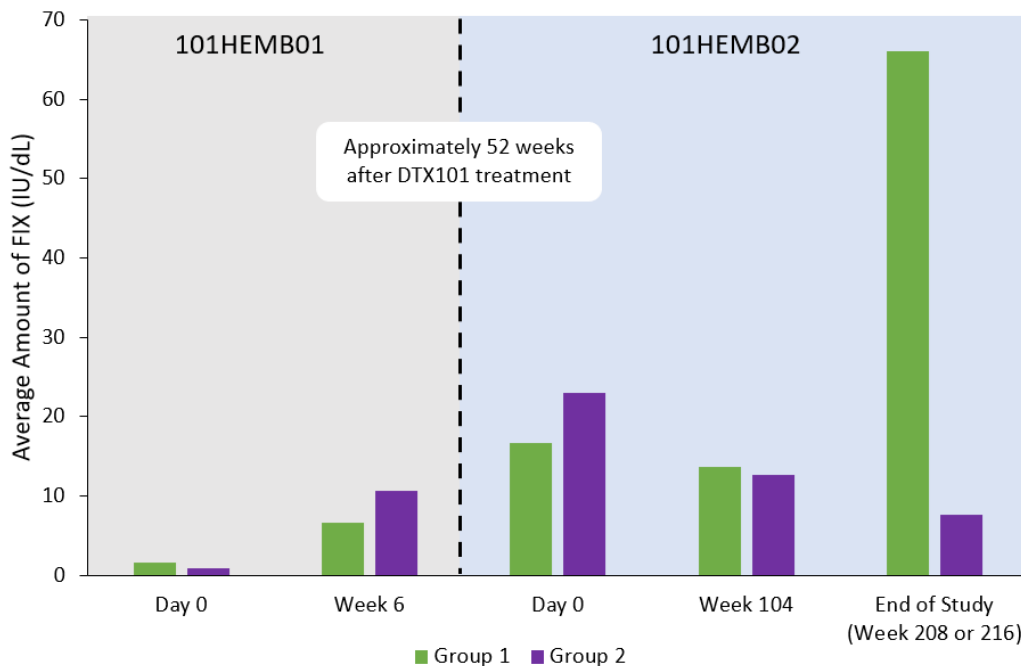


Did either dose of DTX101 help patients make the FIX protein?

Yes. Patients who received either dose of DTX101 made more FIX protein than they did before receiving treatment.

To answer this question, researchers looked at the amount of FIX in people's blood at different times after they received DTX101 treatment. The amount of FIX protein was measured per amount of blood in a patient's body, called **IU/dL**. The results of this analysis are shown in the **figure** below.

After being treated with DTX101, patients who received either the lower or higher dose of DTX101 had more FIX in their blood than before treatment. Six weeks after receiving DTX101 the higher DTX101 dose group had more FIX in their blood. At the end of the 101HEMBO2 study, the lower DTX101 dose group had more FIX in their blood than those who received the higher dose. However, it is important to understand that results at the final time point were only available from one patient in the lower dose group.



Patients = 3

3

3

3

1*

Patients = 3

3

3

3

3

* Note: Data was only available from one patient in Group 1 at the End of Study point

What side effects happened during these studies?

What is a side effect?

A **side effect** is an unwanted or unexpected sign or symptom that happens after taking the study treatment.

Side effects may or may not be related to the study treatment, to other drugs taken while in the study, to the patients' medical history, or to any of the tests performed in the study. A lot of research is needed to know if a treatment causes a side effect.



What is a serious side effect?

A side effect is considered **serious** when it:

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

This section is a summary of the side effects that happened during the studies that doctors thought might be related to the study treatment.

What serious side effects did patients with HemB have during this study?

No patients had serious side effects in either study that doctors thought might be related to DTX101.

What other side effects did patients with DTX101 have during this study?

Overall, 67% of patients with HemB (4 of 6) had side effects during the 101HEMB01 study. During the 101HEMB02 study, 17% of patients (1 of 6) had side effects.

The table shows the side effects that happened in the studies that doctors thought might be related to DTX101. None of these side effects were considered serious by doctors:

Side Effect	Group 1 (3 patients)	Group 2 (3 patients)	Total (6 patients)
101HEMB01			
Liver proteins that were too high in the blood (a sign of liver damage)			
Alanine aminotransferase	0	67% (2 patients)	33% (2 patients)
Aspartate aminotransferase	0	33% (1 patient)	17% (1 patient)
Transaminases	0	33% (1 patient)	17% (1 patient)
Feeling tired	33% (1 patient)	0	17% (1 patient)
101HEMB02			
Feeling tired	33% (1 patient)	0	17% (1 patient)

How have the studies helped patients and researchers?

The 101HEMB01 and 101HEMB02 studies showed that both doses of DTX101 helped patients produce more FIX protein.

These results are for the 101HEMB01 and 101HEMB02 studies only. Please talk with your doctor if you have any questions about DTX101.

Following the 101HEMB01 and 101HEMB02 studies, the DTX101 research program has been discontinued. Further clinical research by Ultragenyx is not planned for DTX101. Always talk to a doctor before making any treatment changes.

Where can I learn more about the studies?

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

101HEMB01: <https://clinicaltrials.gov/ct2/show/NCT02618915>

101HEMB02: <https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-003430-25/GB>

Official Study Titles:

101HEMB01: Safety and Dose Finding Study of DTX101 (AAVrh10FIX) in Adults With Moderate/Severe to Severe Hemophilia B

101HEMB02: Long-Term Safety, Tolerability, and Efficacy of DTX101 (AAVrh10FIX) in Adults With Moderate/Severe to Severe Hemophilia B

Clinical Trial numbers:

101HEMB01: NCT02618915/ 2015-001486-67

101HEMB02: NCT02971969 / 2016-003430-25

If you have questions about the results of these studies, 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 patients products for the treatment of rare and ultra-rare diseases, with a focus on serious, debilitating genetic diseases.

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