

The full title of this study is: Bleeding, activity, and safety 3 years after gene transfer with valoctocogene roxaparvovec: Results from GENER8-1

## Plain Language Summary

# Outcomes for men with severe hemophilia A 3 years after treatment with valoctocogene roxaparvovec gene therapy

This infographic was developed and funded by Biomarin. This material is intended for reactive use in response to unsolicited requests from healthcare professionals and patient organizations at International Congresses. For digital use only. Valoctocogene roxaparvovec is not approved for use in Canada, Latin America, Intercontinental or Asia-Pacific regions, or the United States. Roctavian (valoctocogene roxaparvovec) European prescribing information can be found [here](#).

This summary contains information on a scientific abstract and oral presentation given at the International Society on Thrombosis and Haemostasis (ISTH) 2023 congress.



Date of summary: **June 2023**

[View abstract](#)

More information can be found at:  
 • [clinicaltrials.gov/ct2/show/NCT03370913](https://clinicaltrials.gov/ct2/show/NCT03370913)  
 • <https://www.youtube.com/watch?v=NIH0slUPg9A>

## How to say...

**Gene therapy:** jeen THER-uh-pee

**Hemophilia:** hee-muh-FIL-ee-uh

**Prophylaxis:** pro-fil-AC-sis

**Valoctocogene roxaparvovec:** val-octo-CO-jeen roxa-PARVO-vek

## What is the background to this study?

### What is hemophilia A?

- Hemophilia A is a mostly inherited condition that causes affected people to **bleed too easily**
  - An inherited condition is a condition that can be passed down from parent to child
- People with hemophilia A have **missing or low levels** of a blood clotting factor known as **factor VIII (8)**. Factor VIII is a protein that **helps the blood to clot**
  - This means it helps the blood turn from a liquid state to a gel-like state to stop bleeding, for example when you cut yourself
  - People with hemophilia A have a change (called a "mutation") in their DNA, specifically the **F8 gene**. DNA is the body's "instruction book" and "genes" are specific segments of your DNA
  - The F8 gene contains the specific instructions to **make factor VIII**. This change in the F8 gene means that people with hemophilia A cannot make the right amount of working factor VIII
- Without factor VIII it is **more difficult to stop bleeding**. This can affect things like a simple cut but also means that people with hemophilia A bruise easily and can bleed inside the body
- The amount of factor VIII in the blood determines the severity of hemophilia. The lower the amount of factor VIII, the more likely it is that bleeding will occur
- Standard treatment for hemophilia A currently involves replacing missing factor VIII with artificial factor VIII or using treatments that do the same job. These treatments are given by infusion into the blood and might be needed up to several times a week

### Definitions...

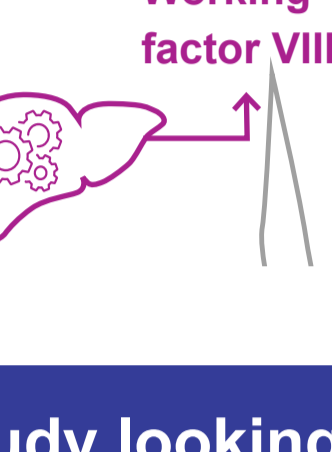
**Normal**  
factor VIII levels are



**Mild hemophilia A**  
factor VIII levels are



**Moderate hemophilia A**  
factor VIII levels are



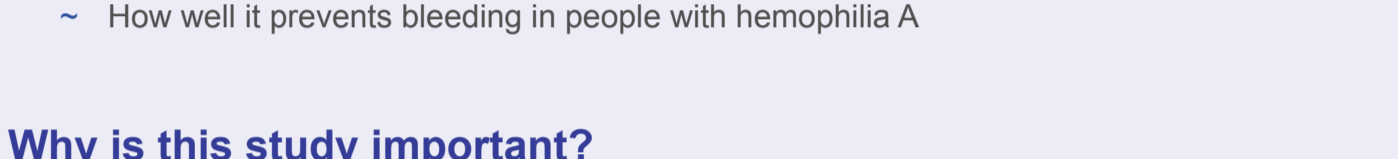
**Severe hemophilia A**  
factor VIII levels are



\*IU/dL means international units per deciliter. This is the standard unit for measuring factor VIII levels and reflects the percentage of normal factor VIII levels (1 IU/dL = 1%)

### What is gene therapy?

Gene therapy is a treatment that delivers instructions, coded by genes, to the patient. This enables them to make working versions of the right proteins.



- Valoctocogene roxaparvovec** is a gene therapy treatment for people with **severe hemophilia A**
- Valoctocogene roxaparvovec** works by transferring **working copies** of the **F8 gene** into liver cells. The F8 gene gives instructions to the liver cells to make working factor VIII proteins



## What is this study looking at?

### What is the aim of this study?

- This study, known as GENER8-1, looks at how well valoctocogene roxaparvovec works for treating people with severe hemophilia A compared with standard treatment with factor VIII replacement
- Researchers have already looked at the results 2 years after gene therapy was given and know that **valoctocogene roxaparvovec can decrease bleeding in severe hemophilia A**
- Researchers want to know:
  - If gene therapy will have long-lasting benefits on factor VIII levels
  - How well it prevents bleeding in people with hemophilia A

### Why is this study important?

- Gene therapy aims to give people with hemophilia A the ability to **make their own working factor VIII**. This means they might not have to rely on replacing factor VIII with regular injections (known as "prophylaxis"), which is the current standard treatment
  - "Prophylaxis" means using a treatment to try to prevent disease. In hemophilia A, this means giving factor VIII infusions in advance to try to help the blood clot in order to stop bleeding

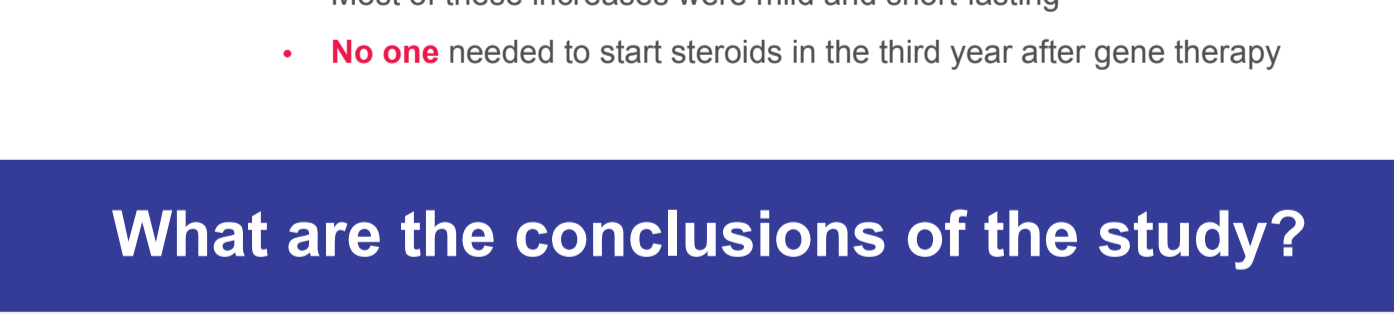
## Who is taking part in this study?

### Adult men (aged over 18):

- With **severe hemophilia A**
- Who had been receiving regular factor VIII infusions for at least 1 year before the study started
- Living in one of the countries included in this international study: Australia, Belgium, Brazil, France, Germany, Israel, Italy, Republic of Korea, South Africa, Spain, Taiwan, the UK, and the US

### NOT included:

- Men with certain proteins in their blood that could affect how well the treatment would work, such as:
  - The body produces against factor VIII (sometimes referred to as "inhibitors")
  - Proteins against the vector that carries the gene in/through the body
- Men with liver problems
- Men with HIV (researchers excluded men with HIV after the start of the study)

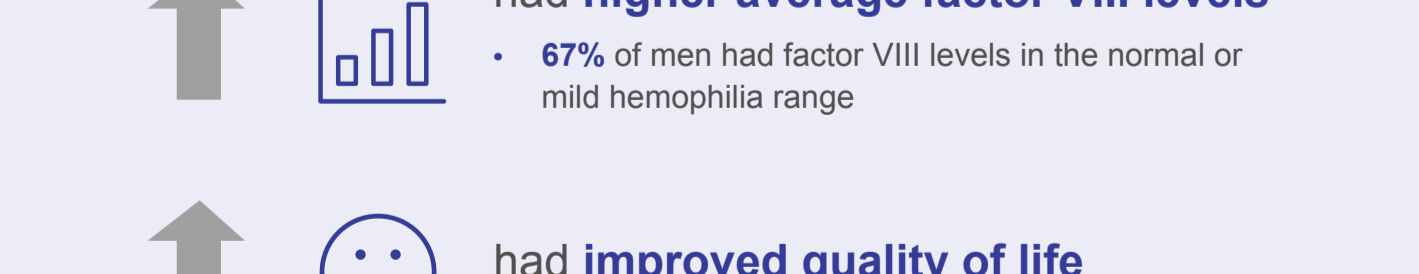


## What are the researchers measuring?

### How WELL the gene therapy works

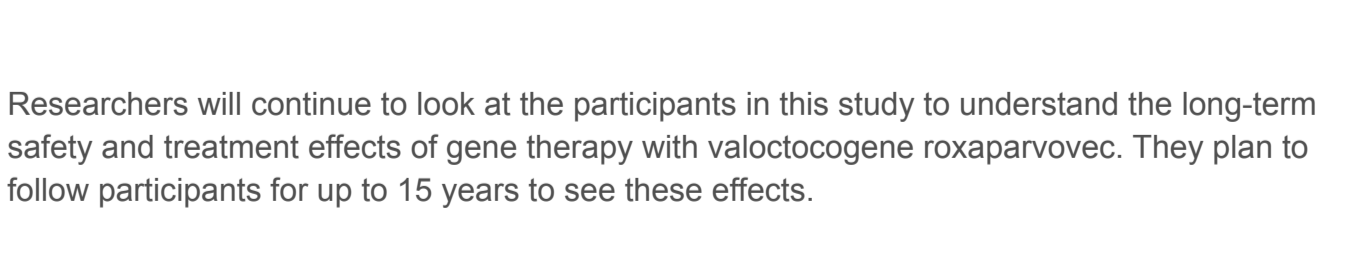


### How SAFE the gene therapy is



## What are the results of the study so far?

By the end of 3 years of treatment, men who received a single dose of valoctocogene roxaparvovec continued to have **improved control of bleeding**.

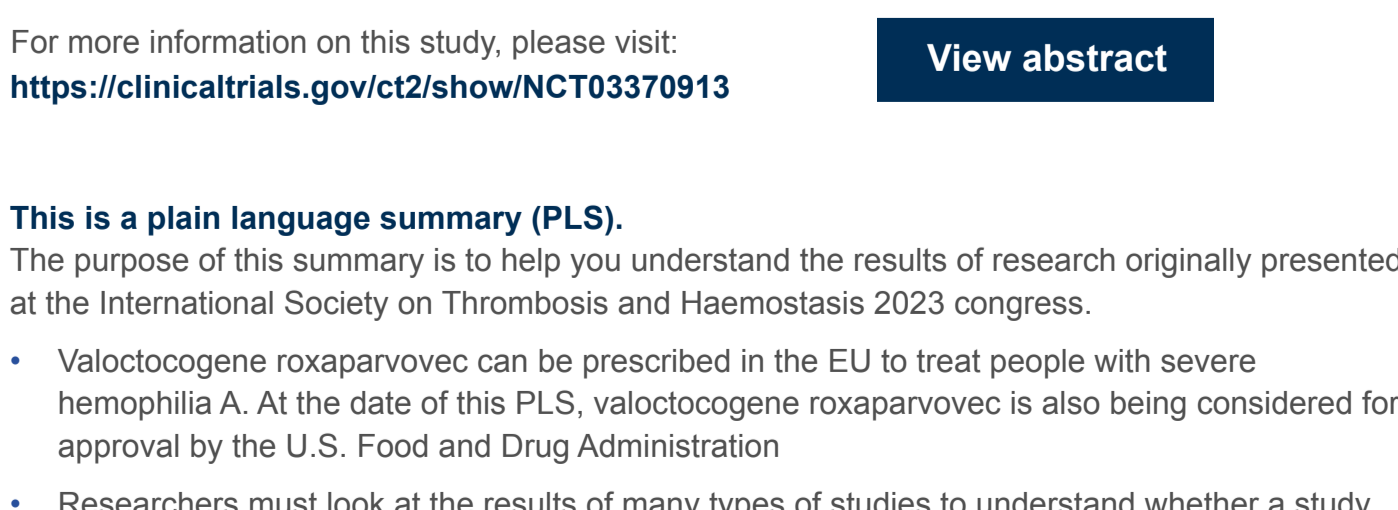


**Only 17 out of 131 men still in the study have returned to regular factor VIII infusions ("prophylaxis") so far**

Men decided to return to prophylaxis for different reasons, including bleeding rates, factor VIII levels and personal preference.

3 years after gene therapy, the average number of bleeds per year that needed treatment decreased from almost **5** before treatment to **1**

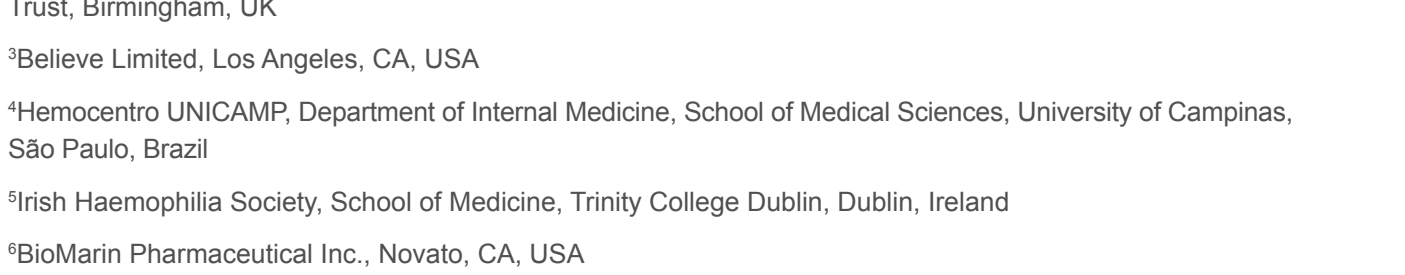
### Number of treated bleeding episodes per year:



### Did valoctocogene roxaparvovec reduce the number of factor VIII infusions needed?



### Did valoctocogene roxaparvovec increase the patient's own factor VIII levels?



### Did treatment with valoctocogene roxaparvovec improve quality of life for people with hemophilia A?

Quality of life was measured using a scoring system out of 100. The score includes how well participants can do their day-to-day activities, how well they can move, and how easy it is to cope with bleeding.

Average **quality of life scores improved** to a level agreed to be important to patients living with hemophilia A

The biggest improvement in quality of life was because of **reduced bleeding**, meaning that men found it easier to cope with their condition

## What were the side effects?

### Most side effects happened in the first year after treatment and were mild.

The most common side effect was an **increase in liver enzyme levels**. An enzyme is a protein that speeds up chemical reactions and is needed for many processes in the body.

- Liver enzymes increased because of an immune response to the valoctocogene roxaparvovec and were treated with medication, usually **steroids**, to suppress this immune response. An "immune response" is the way the body defends itself against substances that it sees as harmful or foreign
- 25% of men had at least 1 episode of raised liver enzyme levels in the third year after treatment
- Most of these increases were mild and short-lasting
- No one** needed to start steroids in the third year after gene therapy

## What are the conclusions of the study?

Compared with standard treatment with regular factor VIII infusions, 3 years after receiving gene therapy, men with hemophilia A:

↓ had **fewer bleeding episodes**  
 • There was an **83%** decrease in yearly bleeding rate

↓ needed **fewer factor VIII infusions** to treat bleeds  
 • There was a **97%** decrease in yearly factor VIII use

↑ had **higher average factor VIII levels**  
 • **67%** of men had factor VIII levels in the normal or mild hemophilia range

↑ had **improved quality of life**

This means that valoctocogene roxaparvovec was effective for **3 years after treatment**.

## Are there any plans for further studies?

Researchers will continue to look at the participants in this study to understand the long-term safety and treatment effects of gene therapy with valoctocogene roxaparvovec. They plan to follow participants for up to 15 years to see these effects.

## Supporting information

### Who sponsors this study?

This study is sponsored by BioMarin Pharmaceutical Inc.  
 BioMarin Pharmaceutical Inc. Novato, CA.

The sponsors would like to thank everyone who took part in this study.

### Where can I find more information?

For more information on this study, please visit:  
<https://clinicaltrials.gov/ct2/show/NCT03370913>

[View abstract](#)

### This is a plain language summary (PLS).

The purpose of this summary is to help you understand the results of research originally presented at the International Society on Thrombosis and Haemostasis 2023 congress.

- Valoctocogene roxaparvovec can be prescribed in the EU to treat people with severe hemophilia A. At the date of this PLS, valoctocogene roxaparvovec is also being considered for approval by the U.S. Food and Drug Administration
- Researchers must look at the results of many types of studies to understand whether a study drug works, how it works, and whether it is safe to prescribe to patients
- This summary reports the results of only one study. The results of this study may be different from the results of other studies that researchers look at
- This PLS is not peer-reviewed, which means it has not gone through the process of review by other researchers that is often required for publication in a scientific journal

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#### Author conflicts of interest:

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