Plain Language Clinical Study
Summary

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine Studied: No research medicine was given in this study

Protocol Number: C0371004

Dates of Study: 26 July 2018 to 13 December 2024

Title of this Study: A Study to Learn About the Efficacy and Safety of Preventive Routine Replacement Treatment with Blood Clotting Factor IX (9) in Men with Hemophilia B

[An Open Label, Non-Investigational Product, Multi-Center, Lead-in Study to Evaluate Prospective Efficacy and Selected Safety Data of Current Factor IX (FIX) or Factor VIII (FVIII) Prophylaxis Replacement Therapy in the Usual Care Setting of Moderately Severe to Severe Adult Hemophilia B Participants (FIX:C≤2%) Who are Negative for Neutralizing Antibodies to Adeno-Associated Virus Vector-Spark100 (Benegene-1) and Moderately Severe to Severe Hemophilia A Adult Participants (FVIII:C≤1%) Who are Negative for Neutralizing Antibodies to

Adeno-Associated Virus Vector 6 (AAV6), Prior to the Respective Therapeutic Phase 3 Gene Therapy Studies]

Date of this Report: 16 July 2025

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.

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Why was this study done?

What is hemophilia B?

Hemophilia B is a usually inherited bleeding disease that mainly affects men. It happens due to lack of a protein which helps in blood clotting. This protein is called blood clotting Factor IX (9) or FIX. People with hemophilia B can bruise easily. They are more likely to bleed for longer than normal after a cut or an injury. This is because it is difficult to form a blood clot to stop the bleeding. Bleeding events may also happen inside the body, affecting different parts of the body, such as joints or muscles.

Hemophilia B is said to be severe when "factor IX activity" levels in the blood are below 1%. It is said to be moderately severe when factor IX activity levels are between 1% and 2%. The normal range of factor IX activity levels is between 50% to 150%. Factor IX activity levels tell how well factor IX is working in the body to help blood to clot.

Currently, the treatment for hemophilia B includes replacement of factor IX when needed, or at regular scheduled intervals (prophylaxis), to help stop or prevent bleeding events. The replacement treatments are given as an injection into a vein. The regular and frequent need for factor IX replacement affects the quality of life of people with hemophilia B.

A new way of treating hemophilia B with factor IX is called "gene therapy". A gene carries information that determines how your body looks and functions. In patients with hemophilia B, the gene that carries the information for factor IX does not work properly. As a result, factor IX is either missing or does not work. In hemophilia B gene therapy works by adding a factor IX "gene" directly into the liver cells. The liver cells can then make working factor IX that goes into the blood to prevent bleeding events.

To transfer the gene, a transport tool called 'vector' is used. A vector is being used in a following study with hemophilia B patients. The vector cannot cause disease. It only works as a transport. Gene therapy may reduce the need of frequent factor IX replacement treatment to prevent bleeding events.

What is the medicine studied?

In this study, participants did not receive research medicine. All the participants remained on their current routine and schedule, with prophylaxis factor IX replacement treatment. Prophylaxis means the participants had routine preventive factor IX replacement treatment to prevent a bleeding event.

What was the purpose of this study?

- The researchers wanted to learn about the efficacy and safety of routine preventive factor IX replacement treatment to manage bleeding events in people with hemophilia B.
- This study will be used to provide information for a Phase 3 study where hemophilia B patients are treated with gene therapy. Phase 3 studies are clinical studies to learn about the efficacy and safety of a research medicine.

Researchers wanted to know:

How many bleeding events happened in participants who received routine preventive factor IX replacement treatment during the study?

What happened during the study?

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How was the study done?

During several months, researchers observed a group of study participants following their routine preventive replacement treatment with factor IX to find out how many bleeding events happened during the study.

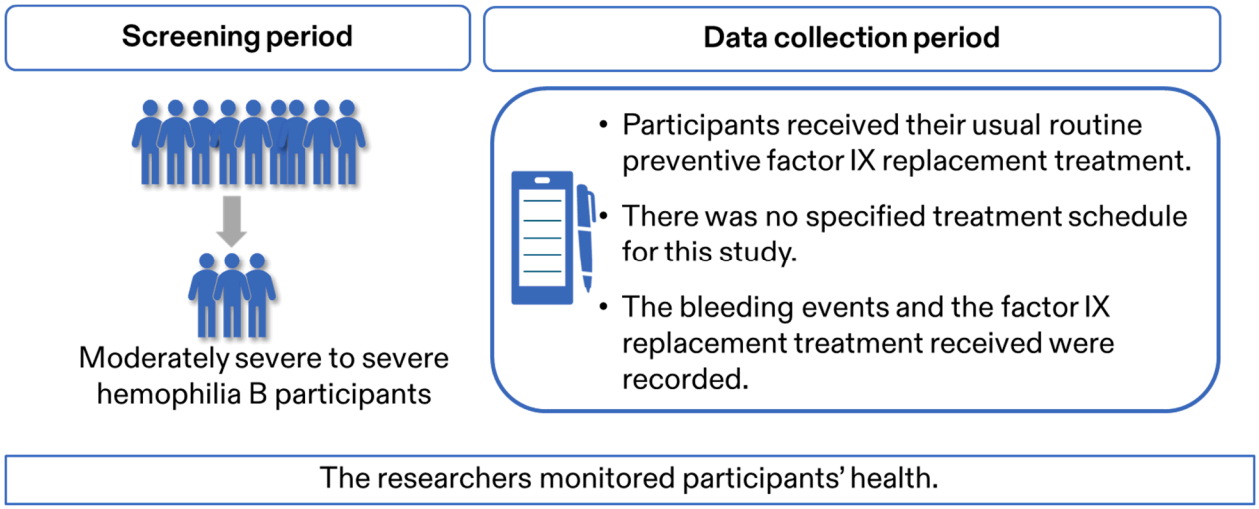
This was an “open label” study, in which both the researchers and the study participants knew about the factor IX replacement treatment being given.

The study had two periods: Screening period and Data Collection period, as shown in Figure 1.

During the Screening period, the researchers checked who could take part in this study. During the Data Collection period, the participants who were already on routine preventive factor IX replacement treatment were asked to record their bleeding events and factor IX replacement treatment received in an electronic diary (e-Diary) through the end of their participation in the study. There was no specified treatment schedule for this study. The participants continued to receive their usual routine preventive factor IX replacement treatment.

The researchers monitored participants’ health throughout the study.

Figure 1: What happened during the study



Where did this study take place?

The Sponsor ran this study at 65 locations in 18 countries in Australia, Asia, Europe, Middle East, North America, and South America.

When did this study take place?

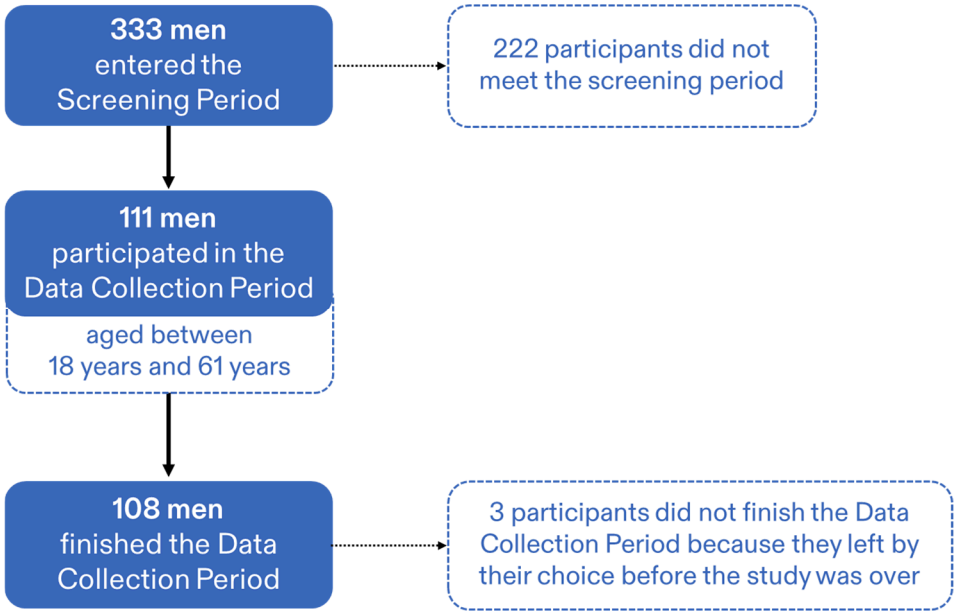
It began on 26 July 2018 and ended on 13 December 2024.

Who participated in this study?

The study included participants who had moderately severe or severe hemophilia B. They were on stable factor IX replacement therapy as a routine preventive treatment with at least 50 "exposure days" of factor IX treatment. Exposure days are the number of calendar days on which a person receives one or more injections of factor IX replacement therapy. They had no significant liver disease. They did not have any "antibodies" that could interfere with factor IX replacement treatment (factor IX inhibitors). Antibodies are substances your body uses to fight off an infection or foreign things like bacteria or viruses. Sometimes the body sees the replacement factor IX as a foreign substance and produces antibodies to destroy it. These inhibitors could prevent replacement

factor IX treatment from working. Participants did not have any antibodies against vector to be used in the Phase 3 study. If antibodies against vector are present, they will not allow the vector to deliver the gene to the liver cells to make factor IX, when participants receive it in a Phase 3 study. Figure 2 shows the number of participants in the study.

Figure 2: The number of participants in the study



How long did the study last?

Most study participants who enrolled in the study were expected to spend at least 6 months in the Data Collection period. Participants remained in the study until everything was ready for them to enter the Phase 3 study at a clinical site. Overall, the study participants were in the Data Collection period for an average of 1 year and 4 months. The entire study took 6 years and 5 months to complete.

When the study ended in December 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How many bleeding events happened in participants who received routine preventive factor IX replacement treatment during the study?

For this study, researchers used the available data from the patients' e-Diary to find out the average number of bleeding events that can happen in a year.

It was found that the average number of all the bleeding events over 1 year was approximately 4.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medicine might have on a participant.

Twenty-two (22) out of 111 participants (20%) in this study had at least 1 medical problem. No participants left the study because of medical problems. The most common medical problems – those reported by more than 1 participant – are described below in Table 1.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 1 participant are listed.
- The **2nd** column tells how many of the 111 participants taking the routine preventive factor IX replacement treatment reported each medical problem. Next to this number is the percentage of the 111 participants who took the factor IX replacement treatment and reported the medical problem.
- Using these instructions, you can see that 2 out of the 111 participants (2%) receiving the routine preventive factor IX replacement treatment reported bleeding in the stomach or gut.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Routine Preventive Factor IX replacement treatment (111 Participants)**
Bleeding in the stomach or gut	2 out of 111 participants (2%)
Collection of blood under the skin	2 out of 111 participants (2%)
Joint pain	2 out of 111 participants (2%)
Sprained ligament	2 out of 111 participants (2%)

Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

Nine (9) out of 111 participants (8%) had serious medical problems.

Of these 9 participants, 2 participants reported bleeding in the stomach/gut. Additionally single occurrences of the following serious medical problems were reported:

- inflammation of the small intestine (a part of the gut);
- joint injury and worsening of damage to the joints;
- broken tooth;

- inflammation of the appendix;
- ligament rupture and sprain;
- damage to joints due to hemophilia and
- swelling and irritation of the lungs.

No participants died during the study.

Where can I learn more about this study?

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

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C0371004**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT03587116**
www.clinicaltrialsregister.eu	Use the study identifier **2017-001271-23**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the best ways to help patients, and you helped us to do that!

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