Clinical Study Results

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 medication 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: 17 September 2019 to 24 July 2023

Title of this Study: A study to learn about the efficacy and safety of preventive routine replacement treatment with blood clotting factor VIII (8) in adults with hemophilia A

[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(s) of this Report: 16 May 2024

– 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. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is hemophilia A?

Hemophilia A is an 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 VIII (8) or FVIII. People with hemophilia A 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 A is said to be severe when “FVIII activity” levels in the blood are below 1%. It is said to be moderately severe when FVIII activity levels are exactly 1%. The normal range of FVIII activity levels is between 50% to 150%. FVIII activity levels tells how well FVIII is working in the body to help blood to clot.

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

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

To transfer the gene, a transport tool called ‘vector’ is used. In this study, a viral vector called adeno-associated virus 6 (AAV6) was used. The vector cannot cause disease. It only works as a transport. Gene therapy may reduce the need of frequent FVIII replacement treatment to prevent bleeding events.

What is the medicine studied?

In this study, participants received no research medicine. All the participants remained on their current routine and schedule with preventive FVIII replacement treatment.

What was the purpose of this study?

- The researchers wanted to learn about the efficacy of routine preventive FVIII replacement treatment to manage bleeding events in people with hemophilia A.
- They also wanted to learn about the safety of routine preventive FVIII replacement treatment.
- This study will be used to provide information for a phase 3 study where hemophilia A 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 FVIII replacement treatment during the study?

What happened during the study?

How was the study done?

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

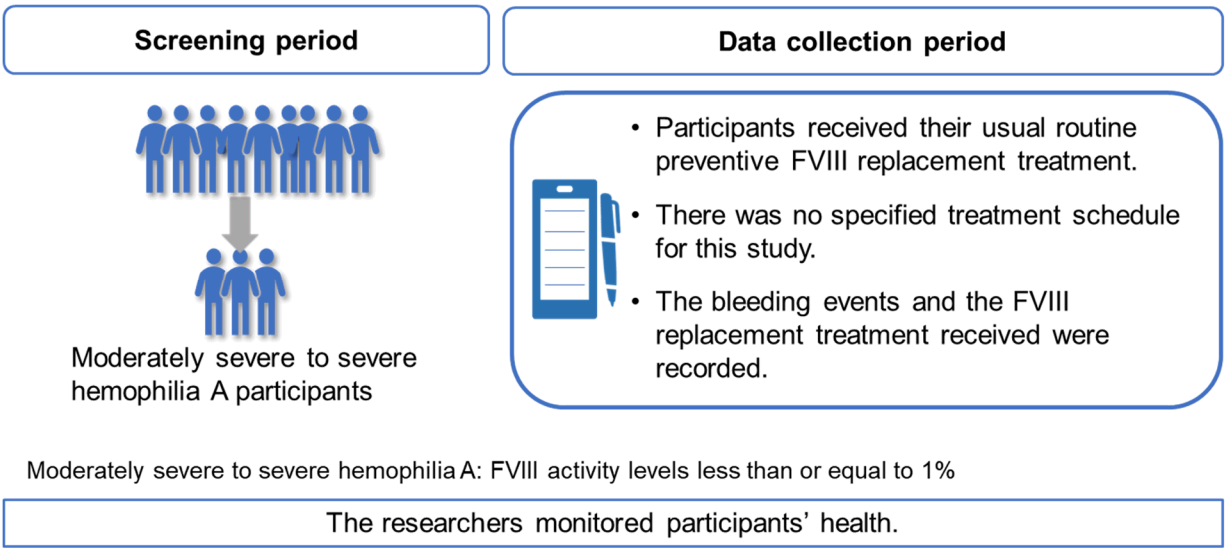
This was an “open label” study, in which both the researchers and the study participants knew the treatment being given.

The study had two periods: Screening period and Data Collection period (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 FVIII replacement treatment were asked to record their bleeding events and FVIII replacement treatment received in an electronic diary (eDiary) 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 FVIII 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 35 locations in 18 countries in Australia, Asia, Europe, Middle East, North America, and South America.

When did this study take place?

It began 17 September 2019 and ended 24 July 2023.

Who participated in this study?

The study included participants who had moderately severe or severe hemophilia A. They were on stable FVIII replacement therapy as a preventive treatment with at least 150 days of earlier exposure to FVIII treatment. They had no significant liver disease. They did not have any "antibodies" that could interfere with FVIII replacement treatment (FVIII inhibitors). Antibodies are substance your body uses to fight off an infection or foreign things like bacteria or viruses. Sometimes the body sees the replacement FVIII as a foreign substance and produces antibodies to destroy it. These FVIII inhibitors could prevent treatment from

working. Participants did not have any antibodies against viral vector AAV6. If antibodies against AAV6 are present, they will not allow the vector to deliver the gene to the liver cells to make FVIII.

- A total of 101 men participated.
- All participants were between the ages of 18 and 64 years, as required for this study. The average age of participants was 32 years.

Participants were to be treated until the end of the data collection period for this study. Of the 101 participants who started the study, 99 finished the data collection period.

Two participants did not finish the data collection period because:

- One participant was no longer available for follow-up.
- One participant no longer met the study requirement for participation.

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 10 months. The entire study took 3 years and 10 months to complete.

When the study ended in July 2023, 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 FVIII replacement treatment during the study?

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

It was found that the average number of bleeding events over one year was approximately 6.

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 medication might have on a participant.

Nine (9) out of 101 (9%) participants in this study had at least 1 medical problem. One (1) participant left the study because of medical problems. All medical problems reported by 9 participants 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 participants are listed.
- The **2nd** column tells how many of the 101 participants taking the preventive FVIII replacement treatment reported each medical problem. Next to this number is the percentage of the 101 participants taking the preventive FVIII replacement treatment who reported the medical problem.
- Using these instructions, you can see that 1 out of the 101 (1%) participants receiving the routine preventive FVIII replacement treatment reported bleeding in the food pipe or stomach.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Preventive FVIII replacement treatment (101 Participants)**
Bleeding in the food pipe or stomach	1 out of 101 participants (1%)
Bleeding of joint	1 out of 101 participants (1%)
Bleeding of hemorrhoids (Hemorrhoids are swollen veins in the lower rectum and anus)	1 out of 101 participants (1%)
Broken hand	1 out of 101 participants (1%)
Cancer of white blood cells, involved in the body's defenses	1 out of 101 participants (1%)
Depression	1 out of 101 participants (1%)
Infection of the wound	1 out of 101 participants (1%)
Muscle pain	1 out of 101 participants (1%)
Pain in throat or mouth	1 out of 101 participants (1%)
Pressure on or stretching of nerve at the elbow	1 out of 101 participants (1%)

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.

Four (4) participants (4%, or 4 out of 101 participants) had serious medical problems.

- One (1) participant had bleeding in the food pipe or stomach; 1 had bleeding of hemorrhoids; 1 had an infection of a wound and 1 had cancer of white blood cells, involved in the body’s defenses.

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!