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(s) Studied: Giroctocogene fitelparvovec

Protocol Number: C3731001

Dates of Study: 21 June 2017 to 16 July 2024

Title of this Study: A Study to Assess the Safety and Tolerability of PF-07055480/Giroctocogene Fitelparvovec Gene Therapy in Adults With Severe Hemophilia A

(A Phase 1/2, Open-Label, Adaptive, Dose-Ranging Study to Assess the Safety and Tolerability of SB-525 [PF-07055480] [Recombinant AAV2/6 Human Factor 8 Gene Therapy] in Adult Subjects With Severe Hemophilia A)

Date(s) of this Report: 07 April 2025

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– 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 A?

Hemophilia A is an inherited bleeding disease that mainly affects men. It happens due to lack of a protein that helps blood to clot. This protein is called blood-clotting factor VIII (8) or "FVIII". Depending on its severity, people with hemophilia A can bruise or bleed 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.

Measuring FVIII activity levels in the blood tells doctors how well FVIII is working in the body to help blood to clot. Hemophilia A is said to be severe when FVIII activity levels in the blood are very low (less than 1% of normal). The normal range of FVIII activity levels in the blood is between 50% and 150%.

What is giroctocogene fitelparvovec?

Giroctocogene fitelparvovec is pronounced "jeer-octo-KOH-jeen fi-tell-PAHR-voh-vec".

A gene carries information that determines how your body looks and functions. In people with hemophilia A, the gene that carries the information for FVIII does not work properly. As a result, in hemophilia A, FVIII is either missing or does not work. 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. Giroctocogene fitelparvovec is a "gene therapy" that is being investigated as a new way of treating hemophilia A with FVIII.

To transfer the gene, a transport tool called a "vector" is used. In this study, a viral vector called "adeno-associated vector 6" (AAV6) was used. The viral vector cannot cause disease. It only works as transport to carry the specific gene into

the target liver cells. Introducing a working copy of the FVIII gene may allow the liver cells to produce FVIII. In this way, giroctocogene fitelparvovec may reduce the need for frequent FVIII replacement treatments to prevent bleeding events.

Giroctocogene fitelparvovec is given as a drip, directly and slowly into a person's vein by a needle, over several hours. It is a 1-time treatment.

What was the purpose of this study?

The purpose of this study was:

- To look at how levels of FVIII changed in the blood after a single treatment of giroctocogene fitelparvovec and how levels of FVIII changed depending on the dose given.
- T*o assess the safety of a single treatment of giroctocogene fitelparvovec.*

Researchers wanted to know:

- **What effect did taking different doses of giroctocogene fitelparvovec have on the amount of FVIII in the blood?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested giroctocogene fitelparvovec on a group of study participants to look at the safety and to find out the effect of giroctocogene fitelparvovec on levels of FVIII in the blood. Researchers tested different doses of giroctocogene

fitelparvovec in different participants. They did this to see how different doses affected the levels of FVIII in the blood.

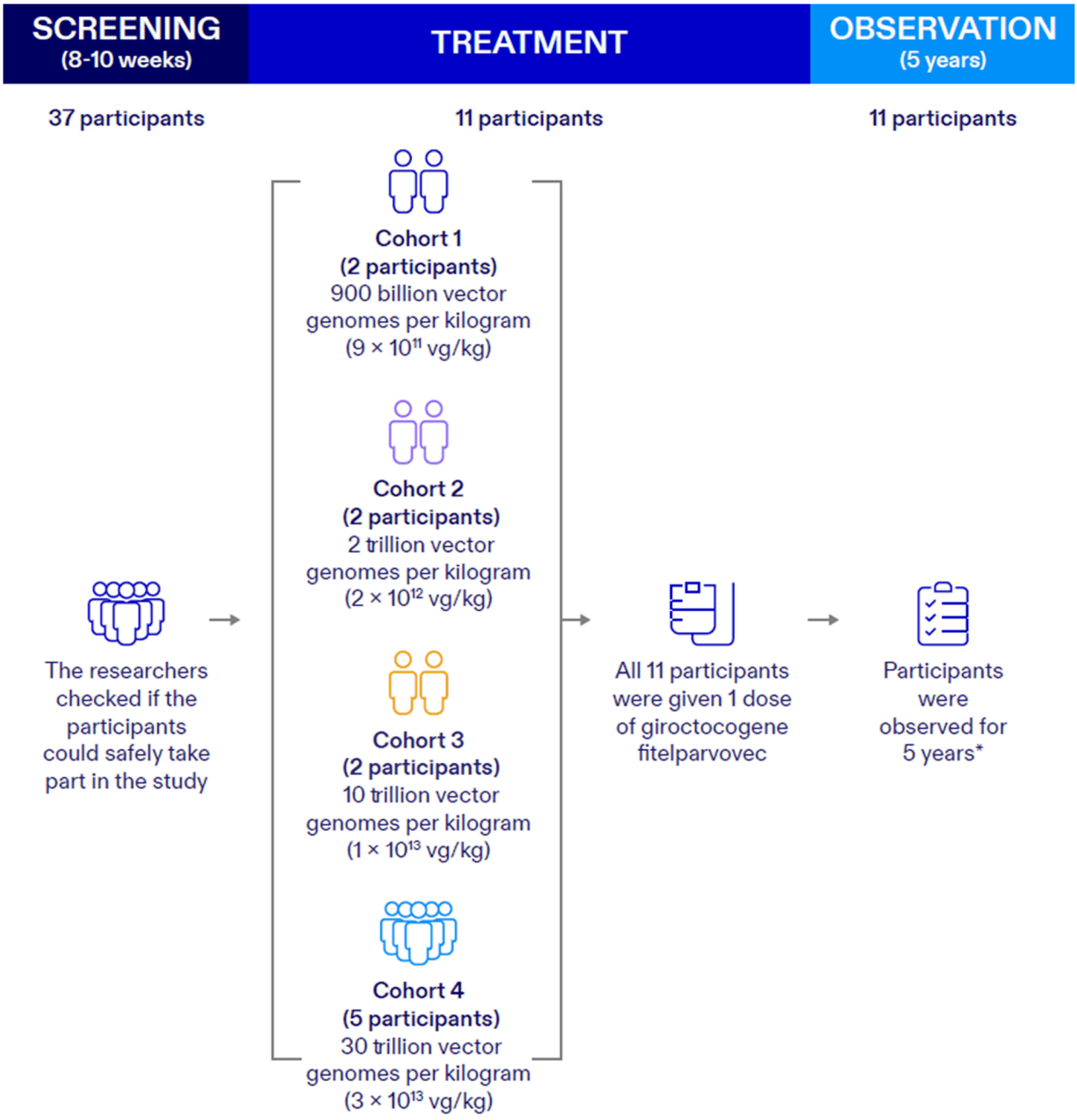
First, researchers checked each participant to make sure they were able to join this study. This is known as screening.

The participant was then given a dose of giroctocogene fitelparvovec. The dose they were given depended on which group or cohort they had been assigned to. There were 4 groups. Each group received a dose of giroctocogene fitelparvovec at increasing amounts of vector genome per kilogram bodyweight (vg/kg for short). Vector genome is the unit used to describe how many vector particles are given. Cohort 1 received the lowest dose, followed by Cohort 2 and Cohort 3. Cohort 4 received the highest dose. The doses given ranged from 900 billion vector genomes per kilogram (9×10^{11} vg/kg) in Cohort 1 to 30 trillion vector genomes per kilogram (3×10^{13} vg/kg) in Cohort 4. Study participants were assigned to a group randomly, like rolling a dice.

Participants received 1 dose of giroctocogene fitelparvovec. Both the researchers and the participants knew the treatment being given. This is called an "open-label" study.

After treatment, the researchers monitored the participants' health for 5 years (60 months). Participants were given an electronic diary (eDiary) where they could record any bleeding events or any treatment with FVIII replacement therapy. Researchers could then use this information to assess whether the number of bleeding events or use of FVIII replacement therapy had changed after treatment with giroctocogene fitelparvovec. Blood tests were also done to check the safety of giroctocogene fitelparvovec and check the levels of FVIII in the blood. Figure 1 shows the study plan.

Figure 1. Study plan



* Not all of the 11 participants completed the 5 years of observation; 8 participants were observed or followed for the full 5 years and 2 participants were followed for 3 years.

Where did this study take place?

The Sponsor ran this study at 6 locations in the United States.

When did this study take place?

It began 21 June 2017 and ended 16 July 2024.

Who participated in this study?

The study included male participants who were over 18 years of age and had severe hemophilia A. Participants also had no antibodies against AAV6 or against FVIII. Antibodies are what your body makes to fight off an infection, or foreign things like bacteria or viruses. If a participant's body made antibodies against AAV6 these could have stopped AAV6 from delivering the gene to the liver cells. Antibodies against FVIII (also called "FVIII inhibitors") could have stopped the new FVIII from working. The new FVIII means the FVIII that is made as a result of the giroctocogene fitelparvovec treatment.

- A total of 11 men were dosed.
- All participants were between the ages of 18 years and 47 years.

Participants were to be treated once. Of the 11 participants who started the study, 8 participants were observed or followed for the full 5 years, and 2 participants were followed for 3 years. These 2 participants did not sign the consent form to extend the follow-up period for the additional 2 years.

One participant did not finish the study because he was lost to follow-up. This means that the researchers were not able to contact him to ask about his health.

No participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study.

How long did the study last?

Study participants were in the study for 3 years to 5 years after treatment. The entire study took around 7 years to complete.

When the study ended in July 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?

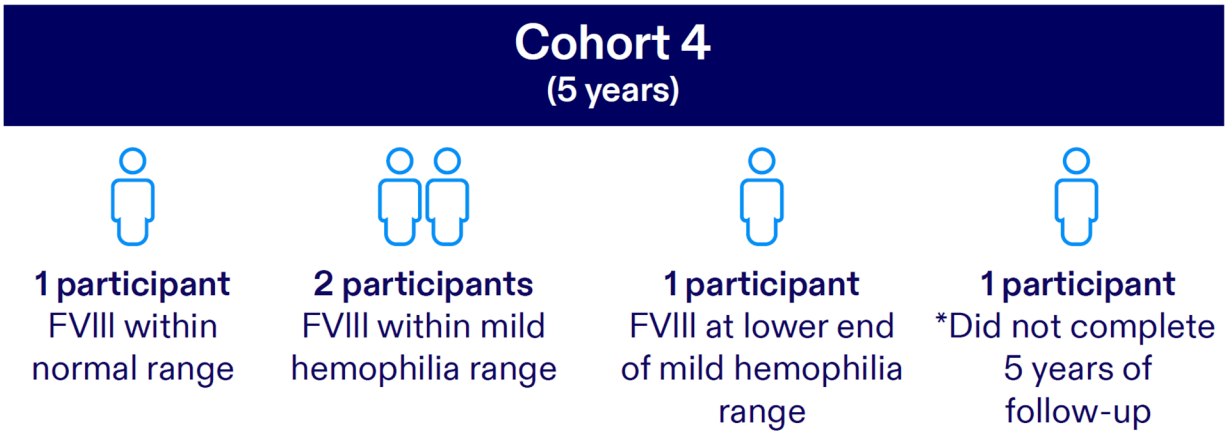
What effect did taking different doses of giroctocogene fitelparvovec have on the amount of FVIII in the blood?

Participants had regular blood tests to measure FVIII in their blood. Researchers measured the amount of FVIII in each of the participant's blood by looking at how well the blood could form clots. Participants in Cohort 4 had the highest levels of FVIII detected in the blood. These participants were those receiving the highest dose of giroctocogene fitelparvovec.

Did taking giroctocogene fitelparvovec change the amount of FVIII in the blood?

In Cohorts 1 and 2, there were no or very low levels of FVIII detected in the participant's blood after treatment. All participants had to resume their FVIII replacement therapy. In Cohort 3, FVIII levels were detected after treatment in both participants. One participant still had detectable levels of FVIII at 5 years. The other participant had to resume FVIII replacement therapy. In Cohort 4, levels of FVIII were within the mild or the normal range in 4 out of 5 participants at the time the participant completed the study. These participants had a low number of bleeding events and a lower need for FVIII replacement therapy. Figure 2 shows the results for participants in Cohort 4.

Figure 2. Cohort 4 results



**This participant completed the study after 3 years and at this time FVIII was within mild hemophilia range*

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.

All 11 participants (100%) 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 2 or more participants – are described below.

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 2 or more participants are listed.
- The **2nd** column tells how many of the 11 participants who took giroctocogene fitelparvovec reported each medical problem. Next to this number is the percentage of the 11 participants who took giroctocogene fitelparvovec and reported the medical problem.
- Using these instructions, you can see that 5 out of the 11 participants (45.5%) who took giroctocogene fitelparvovec reported nose and throat infection.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Giroctocogene Fitelparvovec (11 Participants)
Nose and throat infection	5 out of 11 participants (45.5%)

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Giroctocogene Fitelparvovec (11 Participants)**
Ear infection	2 out of 11 participants (18.2%)
Increased level of a liver protein (enzyme) called "ALT" in the blood	9 out of 11 participants (81.8%)
Increased level of a liver protein (enzyme) called "AST" in the blood	7 out of 11 participants (63.6%)
Low levels of lymphocytes, a type of white blood cell, in the blood	2 out of 11 participants (18.2%)
Cuts on the skin	2 out of 11 participants (18.2%)
Fall	2 out of 11 participants (18.2%)
Mouth and throat pain	2 out of 11 participants (18.2%)
Rapid heartbeat	2 out of 11 participants (18.2%)
Fever	4 out of 11 participants (36.4%)
Joint pain	2 out of 11 participants (18.2%)

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Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Giroctocogene Fitelparvovec (11 Participants)**
A joint disease found in some hemophilia patients called hemophilic arthropathy	2 out of 11 participants (18.2%)
Headache	2 out of 11 participants (18.2%)
Low blood pressure	2 out of 11 participants (18.2%)

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.

Three participants (27.3%, or 3 out of 11 participants) had serious medical problems.

- One (1) participant in Cohort 2 had 2 separate infections of the deep skin tissue. Another participant in this group had a burn. None of these medical problems were considered related to giroctocogene fitelparvovec.
- One (1) participant in Cohort 4 had low blood pressure and fever shortly after receiving treatment. These serious medical problems were considered to be related to the infusion of giroctocogene fitelparvovec and got better with treatment within less than 24 hours.

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 **C3731001**

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

www.clinicaltrials.gov

Use the study identifier **NCT03061201**

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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