# CLINICAL TRIAL 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 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:** Fidanacogene elaparvovec (PF-06838435 [SPK-9001])

**Protocol Number:** C0371005 (previously SPK-9001-101)

**Dates of Trial:** 18 November 2015 to 08 April 2019

**Title of this Trial:** A Gene Therapy Study for Hemophilia B

[Gene Therapy, Open-Label, Dose-Escalation Study of SPK-9001 (Adeno-Associated Viral Vector With Human Factor IX Gene) in Subjects With Hemophilia B]

**Date(s) of this Report:** 22 February 2021

## *– Thank You –*

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

# WHY WAS THIS STUDY DONE?

Hemophilia is a disease that is "inherited", which means it runs in families, and it mainly affects boys and men. People with hemophilia have problems with their blood not clotting. After an injury, someone with hemophilia will bruise more easily and, if cut, will bleed for longer. Sometimes the bleeding can happen inside the body and this "internal bleeding" can be serious as it can cause damage.

Doctors prescribe medicines called "factor replacement therapy" to help the blood to clot in people with hemophilia. These treatments work by replacing the clotting factors that are missing from the blood of a person with hemophilia. Clotting factors are proteins in the blood that help stop bleeding after an injury as well as prevent bleeding from happening. There are many different clotting factors in the blood and these are numbered using Roman numerals. People with hemophilia B are missing Factor IX (9) (FIX). This means FIX is given to people with hemophilia B. Factor replacement therapy is given by "infusion" where the medicine is prepared in a syringe and then "injected" or pushed through a patient's skin into a "vein". A vein is a tube that carries blood around the body. Other treatments are also available that can be given by "injection", or a shot, "subcutaneously", to prevent or reduce the number of bleeding episodes (also known as bleeds). Subcutaneously means the injection is given just underneath the skin.

Fidanacogene elaparvovec is a new kind of treatment being studied for hemophilia. It works in a different way to other treatments to help blood to clot. Fidanacogene elaparvovec is a novel recombinant adeno-associated virus (AAV), which in nature causes no disease, to deliver the human factor IX (hFIX) gene to the liver cells where FIX is normally made.

For this study, researchers were interested in learning about the safety and kinetics (movement through the body) of a single dose of fidanacogene elaparvovec where it may help to prevent or reduce the number of bleeding episodes.

# WHAT HAPPENED DURING THE STUDY?

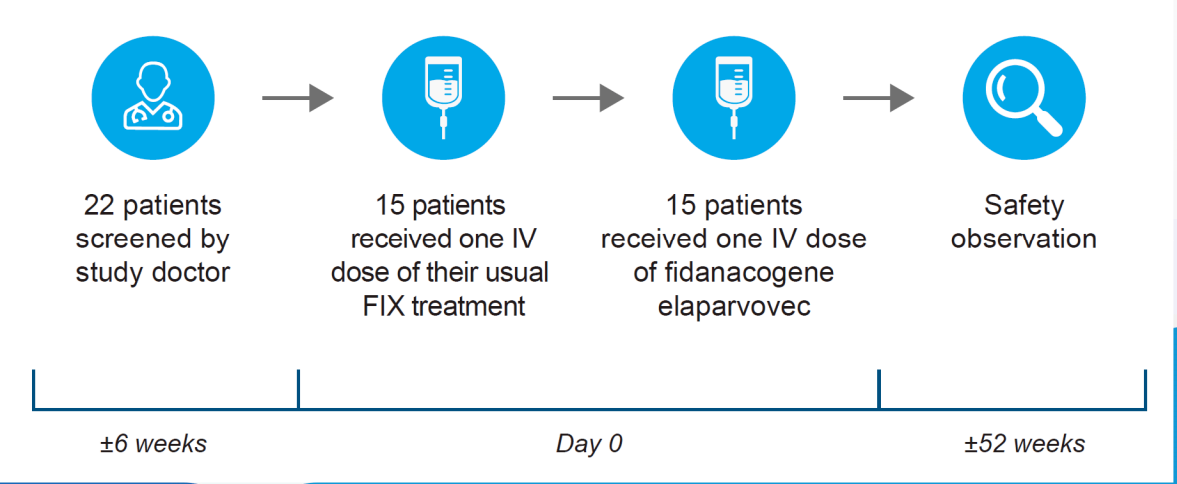
Researchers in this study initially intended to look at 3 groups of patients treated with fidanacogene elaparvovec at 1 of 3 dose levels. This was done to see if patients had any medical problems after this treatment and also see if this treatment could prevent bleeding episodes. Fidanacogene elaparvovec was given as an intravenous (IV) infusion, which means that a needle is placed in the vein and the study drug slowly drips into the vein.

A total of 22 patients were screened, 15 patients received fidanacogene elaparvovec. All 15 patients received the lowest dose in the study ($5 \times 10^{11}$ vg/kg). No patient received the 2 higher doses of fidanacogene elaparvovec. Results presented here are from the lowest dose level.

Patients were treated with 100 IU/kg of their usual FIX protein product over more or less 10 minutes at Day 0 visit. After this, the patients were treated with fidanacogene elaparvovec ($5 \times 10^{11}$ vg/kg) for approximately 60 minutes via infusion pump, as shown in the figure below.

This was an open-label study, so everyone, including the patient, knew what treatment was given.

The study included patients who were men of 18 years of age and older with less than or equal to 2% FIX levels.



While patients were only in the study for 1 year, the entire study took more than 3 years to complete. The Sponsor ran this study at 5 locations in 2 countries (Australia and United States). It began 18 November 2015 and ended 08 April 2019. All patients were men. All patients were between the ages of 18 and 61 years.

Patients were to be treated with a single IV infusion. Of the 15 patients who started the study, all finished the study.

When the study ended in April 2019, 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 much of the standard FIX treatment was absorbed following treatment with fidanacogene elaparvovec?

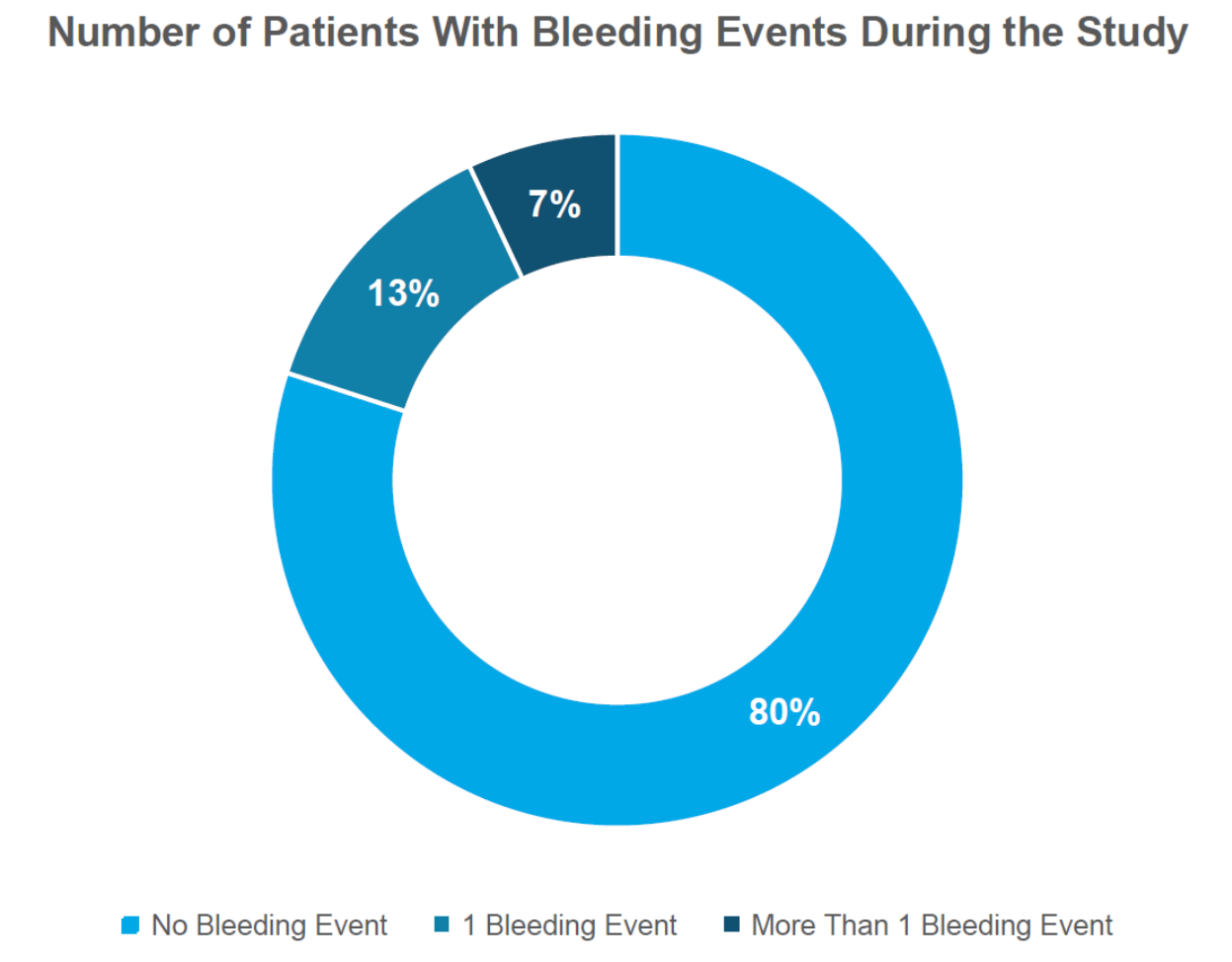
Treatment with fidanacogene elaparvovec did not change the rate at which normal FIX treatment is absorbed.

## Did treatment with fidanacogene elaparvovec have an effect on FIX activity in the body?

During this study, the average FIX activity levels in patients treated with fidanacogene elaparvovec was 23%.

## Did treatment with fidanacogene elaparvovec have an effect on the number of bleeding events for participants?

None of the patients had a traumatic bleed during this study. The average number of bleeding events experienced by the patients, reduced during the 52 weeks in the study, after treatment with fidanacogene elaparvovec. The average bleeding rate for patients treated with fidanacogene elaparvovec, was <1. The amount of bleeding events the patients experienced after fidanacogene elaparvovec treatment, is shown below.




This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

## 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 the side effects of an experimental drug might be.

Fourteen (14) out of 15 patients (93%) in this study had at least 1 medical problem and there were 81 medical problems reported to the study doctors. No patient left the study because of medical problems. The most common medical problems are listed in the table below.

**Most Common Medical Problems (Reported by At Least 20% of Patients)**

| Medical Problem | Fidanacogene Elaparvovec (15 Patients Treated) |
|---|---|
| Nose and throat infection | **5 (33%)** |
| Common cold | **3 (20%)** |
| Back pain | **3 (20%)** |
| Stretched or torn muscle (muscle strain) | **3 (20%)** |

No patient had severe medical problems. Of the 81 medical problems, 53 were mild and 28 were considered moderate.

There were 2 out of 15 patients (13%) who had medical problems that the doctors thought were related to fidanacogene elaparvovec. Both of the treatment-related medical problems that were seen were moderate transaminase elevation, which refers to having high levels of certain liver enzymes, called transaminases, suggesting some inflammation or irritation of the liver.

During the study, patients had blood samples taken for testing. Medical problems identified in these blood tests are described below.

Most of the patients remained generally normal for most laboratory blood tests during the study. One (1) patient experienced 1 moderate medical problem of normocytic anemia (normal-sized red blood cells, but have a low number of them in the body) and 1 patient experienced mild medical problem of microcytic anemia (body has fewer red blood cells than normal and the red blood cells it does have are too small). Both medical problems were considered not related to study drug by the study doctor.

The study doctors did not note any important or study drug-related results in vital signs. There were no physical examination changes after study drug infusion that were important or related to the study drug.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

## WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

No patient had serious medical problems and no patients 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.clinicaltrials.gov | Use the study identifier **NCT02484092** |
| www.clinicaltrialsregister.eu | Use the study identifier **018-003086-33** |

Clinical trials with fidanacogene elaparvovec are ongoing and further trials are planned.

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

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!