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: Marstacimab (PF–06741086)

Protocol Number: B7841002

Dates of Trial: 08 March 2017 to 03 December 2018

Title of this Trial: Study of Marstacimab in Men With Hemophilia [A Multicenter, Open-Label, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of Subcutaneous or Intravenous PF-06741086 in Subjects With Severe Hemophilia]

Date of this Report: 25 November 2019

– 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 in 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 A are missing Factor VIII (8) and people with hemophilia B are missing Factor IX (9). This means Factor VIII is given in factor replacement therapy to people with hemophilia A and Factor IX is given to people with hemophilia B. Factor replacement therapy is given by "infusion" and 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.

Marstacimab (PF-06741086) is a new kind of treatment being studied for hemophilia. It works in a different way to other treatments to help blood to clot. The treatment is given subcutaneously and, over time, the medicine is able to reach the bloodstream where it may help to prevent or reduce the number of bleeding episodes.

WHAT HAPPENED DURING THE STUDY?

This study included 4 groups of patients given an injection of marstacimab at different doses. This was done to see if patients had any medical problems after this treatment and also see if this treatment could prevent bleeding episodes. The 4 groups and the different doses of marstacimab that were given in this study are shown in the following table.

Description of Treatment Groups

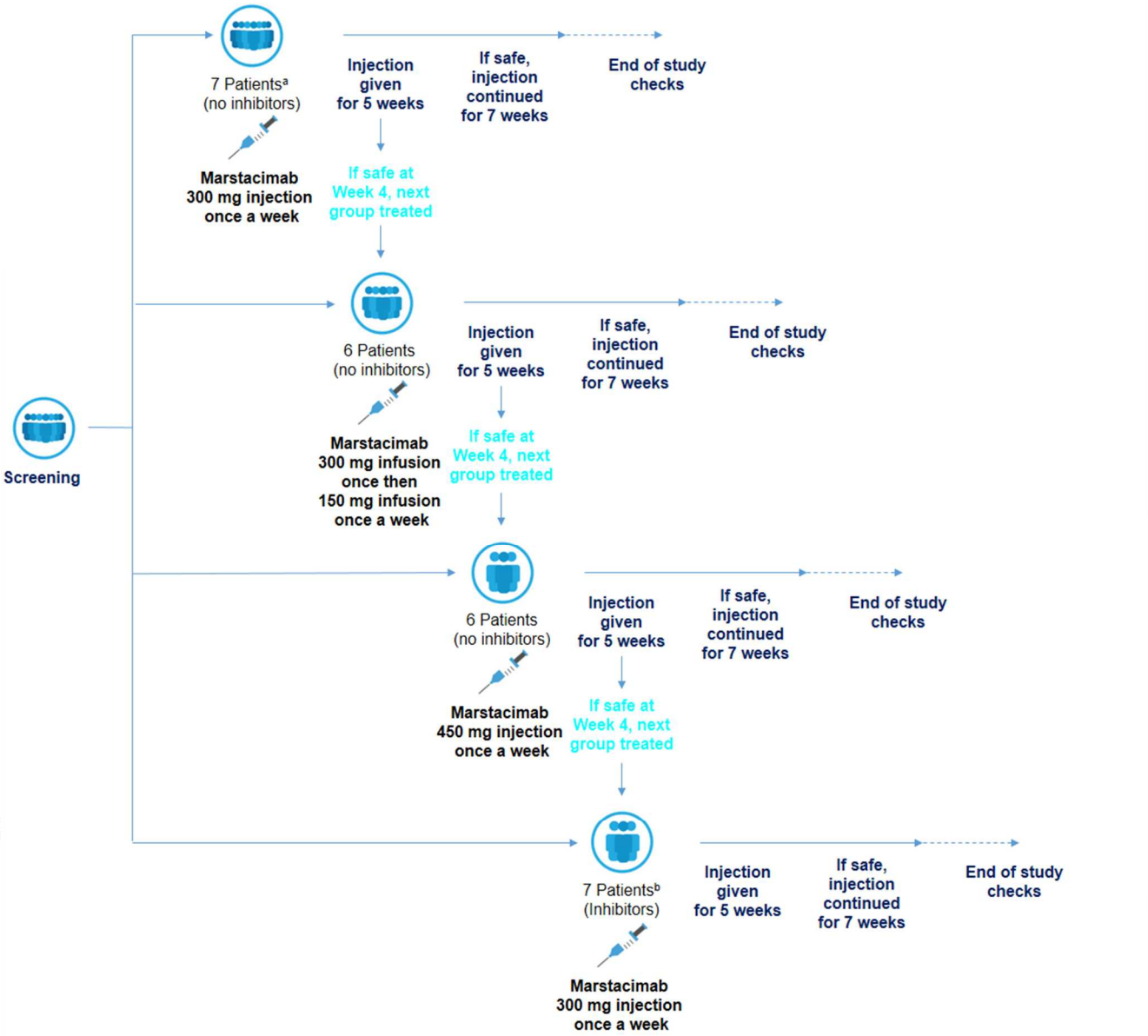
Group	Marstacimab Dose Given	Number of Patients Treated per Group[a]
1	300 mg injection given once a week for 5 weeks (Day 1 to Day 29) and then continued for another 7 weeks (Day 36 to Day 78).	7[a]
If after 4 weeks the treatment in Group 1 went well then patients in Group 2 could be treated.		
2	300 mg injection given once and then 150 mg injection given once a week for 5 weeks (Day 1 to Day 29) and then continued for another 7 weeks (Day 36 to Day 78).	6
If after 4 weeks the treatment in Group 2 went well then patients in Group 3 could be treated.		
3	450 mg injection given once a week for 5 weeks (Day 1 to Day 29) and then continued for another 7 weeks (Day 36 to Day 78).	6
If after 4 weeks the treatment in Group 3 went well then patients in Group 4 could be treated.		
4[b]	300 mg injection given once a week for 5 weeks (Day 1 to Day 29) and then continued for another 7 weeks (Day 36 to Day 78).	7

[a] It was planned that 6 patients would be included in Group 1 and while 8 were enrolled only 7 patients were treated with marstacimab as 1 withdrew their consent before receiving treatment.

[b] Patients with inhibitors to their factor replacement therapy could only join Group 4.

The study included patients who had severe hemophilia A or B, with or without "inhibitors". Some patients with hemophilia can develop inhibitors in their blood to the proteins in factor replacement therapy. These inhibitors stop the clotting factors in the factor replacement therapy from working. This means that people with hemophilia who have these inhibitors may have more severe bleeds and may need higher doses of factor replacement therapy or alternative treatment(s) to stop any bleeding. Patients with inhibitors to their factor replacement therapy were only able to join Group 4.

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



[a] It was planned that 6 patients would be included in Group 1 and while 8 were enrolled only 7 patients were treated with marstacimab as 1 withdrew their consent before receiving treatment
[b] Patients with inhibitors to their factor replacement therapy could only join Group 4.

While patients were only in the study for 5 months, the entire study took 21 months to complete. The sponsor ran this study at 8 locations in 6 countries in North America, South America, Europe and South Africa. It began 08 March 2017 and ended 03 December 2018. 27 men participated and 26 were treated with marstacimab

(1 patient decided he did not want to be treated with marstacimab before being given his first injection). All patients were between the ages of 19 and 63 years.

The 7 patients in Group 1 were treated first and were given 1 injection of marstacimab each week so that they received 5 injections of marstacimab. If these patients did not have many medical problems after 4 weeks, the 6 patients in Group 2 were treated. If the 6 patients in Group 2 did not have many medical problems after 4 weeks, then the 6 patients in Group 3 were treated. If the 6 patients in Group 3 did not have many medical problems after 4 weeks, then the 7 patients in Group 4 were treated.

Patients were to be treated once a week for up to 3 months. Of the 26 patients who started the study, 24 (92%) finished the study and 2 (8%) did not finish the study because of medical problems.

When the study ended in December 2018, 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?

Did patients taking marstacimab have any medical problems?

The researchers recorded any medical problems the patients had during the study. Patients 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 patient 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.

Overall, 21 out of 26 patients (81%) in this study had at least 1 medical problem and there were 56 medical problems reported to the doctors. A total of 2 patients (8%) left the study because of medical problems. This included 1 patient who had high blood pressure and 1 patient who had the level of "fibrinogen" in a blood sample he gave that was reduced after treatment. Fibrinogen is a protein in the blood that is used to make fibrin, which helps blood to clot.

The most common medical problems are listed in the following table.

Most medical problems were not severe (17 out of 21 patients, 81%, had medical problems graded as mild or moderate). There were 4 patients who had medical problems that were severe and these were injection site pain and swelling (2 patients), reduced levels of fibrinogen (1 patient who left the study because of this), and itchy, red rash (1 patient).

Most Common Medical Problems (Reported by 2 or More Patients)	
Medical Problem	**Marstacimab (26 Patients Treated)**
Pain where the injection was given	**3 (12%)**
Swelling where the injection was given	**3 (12%)**
High blood pressure	**3 (12%)**
Increased cardiac troponin (may mean the heart has been injured)	**3 (12%)**
Feeling very tired	**2 (8%)**
Bruising where the injection was given	**2 (8%)**
Hardness around the area the injection was given	**2 (8%)**
Flu (influenza)	**2 (8%)**
Gum disease	**2 (8%)**
Bruising	**2 (8%)**
Prolonged prothrombin time (blood clots too slowly)	**2 (8%)**
Pain in the joints	**2 (8%)**
Headache	**2 (8%)**

There were 14 out of the 26 patients (54%) who had medical problems that the doctors thought were related to marstacimab. Treatment-related medical problems that were seen in 2 or more patients are shown in the following table, with most involving the injection site. Most of the injection site reactions were "mild". This means there was some tenderness around the site of the injection that got better with time and did not need any additional treatment.

Most Common Medical Problems Related to Marstacimab (Reported by 2 or More Patients)	
Medical Problem	**Marstacimab (26 Patients Treated)**
Pain where the injection was given	**3 (12%)**
Swelling where the injection was given	**3 (12%)**
Bruising where the injection was given	**2 (8%)**
Hardness around the area the injection was given	**2 (8%)**
High blood pressure	**2 (8%)**

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

Medical Problems Identified from Blood Tests	
Laboratory Medical Problem	**Marstacimab (26 Patients Treated)**
Abnormal cardiac troponin levels (if increased then may mean the heart has been injured)	**4 (15%)**
Increased cardiac troponin (may mean the heart has been injured)	**3 (12%)**
Prolonged prothrombin time (blood clots too slowly)	**2 (8%)**
Decreased blood fibrinogen (needed for blood clots)	**1 (4%)**

Doctors measured the level of cardiac troponin to see if there has been any damage to the heart and 4 patients had abnormal levels. For 3 of these patients, this was also recorded as increased cardiac troponin. This was thought by doctors to be related to

marstacimab in 2 of these 3 patients. The doctors used an "electrocardiogram", or ECG machine, to look at the activity of the heart during the study. None of the patients had heart problems.

There were 2 patients who had the medical problem of "prolonged prothrombin time" or when the blood clots too slowly. The doctor thought that this medical problem was related to marstacimab treatment in 1 of these 2 patients.

1 patient had their levels of blood fibrinogen, which is needed for blood clots, reduced after treatment and this was thought by the doctor to be related to marstacimab. This patient left the study because of this. While other patients had reduced blood fibrinogen in their blood tests, the doctor did not think these reductions were medically important.

1 of the 26 patients (4%) had a blood pressure increase that the doctor thought was related to marstacimab. This patient left the study because of this.

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.

A total of 4 patients (15%, or 4 out of 26 patients) had serious medical problems. None of these serious medical problems were thought by the doctors to be due to treatment with marstacimab. There were no serious medical problems involving blood clotting. 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 this study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT02974855**
www.clinicaltrialsregister.eu	Use the study identifier **2016-001885-27**

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!