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: Glasdegib

Protocol Number: B1371013

Dates of Trial: 06 October 2014 to 31 October 2018

Title of this Trial: Single-Agent Glasdegib in Patients with Myelofibrosis Previously Treated with Ruxolitinib

[A Phase 2, Double-Blind, Randomized Safety and Efficacy Study of Glasdegib (PF-04449913) versus Placebo in Patients with Myelofibrosis Previously Treated with Ruxolitinib]

Date of this Report: 30 October 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?

What was the purpose of this study?

Myelofibrosis (MF) is a type of bone marrow cancer, characterized by uncontrolled production of abnormal, undifferentiated (stem cells) bone marrow cells leading to development of scar tissue in bone marrow. This can change the body's normal production of blood cells. Clinical features include abnormal blood counts, enlarged spleen and/or liver, bleeding, thrombosis, and debilitating constitutional symptoms such as fatigue, weight loss, night sweats, fever, itchiness, bone pain, abdominal pain, and feeling "full" quicker when eating.

Glasdegib was the medicine tested in this study . Glasdegib has been developed to help reduce the proliferation and growth of abnormal bone marrow stem cells which may allow this cancer to grow. Cancer stem cells are cells that self-regenerate and contribute to tumor growth. The cancer stem cells can lead to tumor resistance to treatment, and spread of the tumor (metastasis). It can also impact a patient's overall survival.

This study was planned to be conducted in two parts: a "Lead-In" phase and a "Randomized" phase. All enrolled patients participated in the "Lead-In" phase of the study only.

The primary purpose of the 'Lead -In' phase of this study was to see if glasdegib (also known as PF-04449913), 100 mg daily dose, taken by mouth, was safe and tolerated in patients with MF who had previously taken ruxolitinib. Ruxolitinib is a medicine, approved for use, to treat MF. Ruxolitinib is sold under the name of Jakafi® or Jakavi®, depending on where you live.

In addition, to determine how their disease responded following 24 weeks of glasdegib study treatment, patients were evaluated to assess if their spleen volume had changed by magnetic resonance imaging (MRI) or computed tomography (CT).

Who was eligible to take part in the study?

The study included adult patients who:

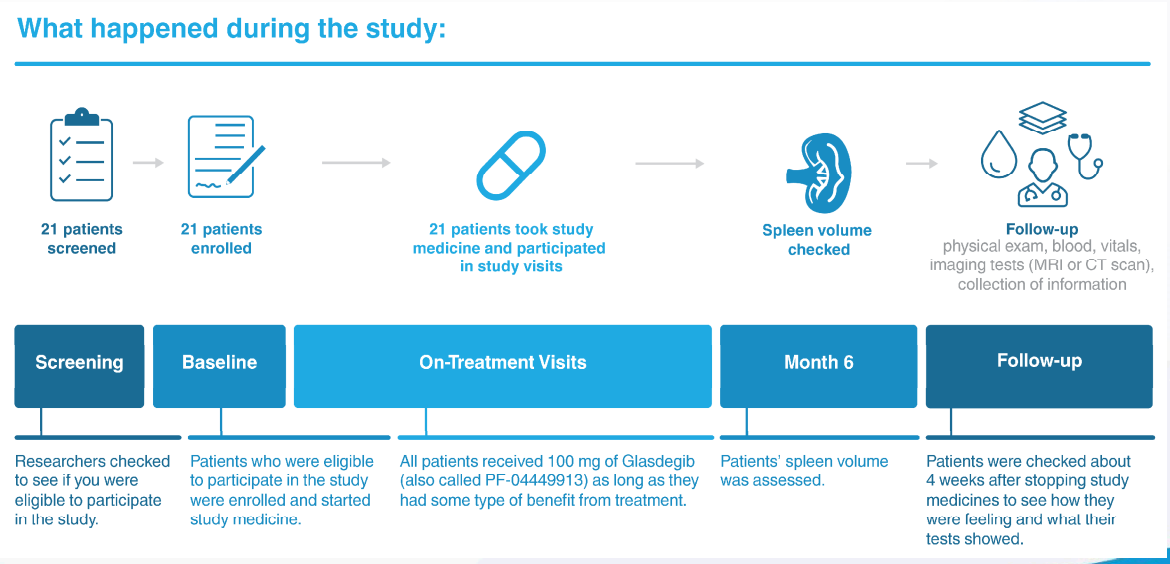
- Were diagnosed with MF;
- Have previously been treated with ruxolitinib for MF, for which they had to stop due to not working well enough, or because it was causing medical problems; and
- Have symptoms of MF
    - Symptoms could include feeling "full" quicker when eating, abdominal discomfort, itchiness, night sweats, bone pain, and shortness of breath.

These were just some of the main criteria patients needed to have to enter the study. There were other criteria to be in the study which are not listed here.

WHAT HAPPENED DURING THE STUDY?

First researchers checked to see if patients were eligible to enter the study at the Screening visit. Next, eligible patients were enrolled into the "Lead In" phase of the study and started the study medicine, glasdegib at the Baseline visit. Over the course of the glasdegib treatment patients were evaluated for safety and remained on treatment for as long as they tolerated and derived clinical benefit from the treatment as determined by their study doctor.

The picture below shows what happened during the study.



Although the safety of glasdegib was considered acceptable in "Lead-In" phase of the study, the study did not proceed into the "Randomized" phase because glasdegib did not appear to reduce the spleen volume.

While patients were only in the study for about 8 months, the entire study took 4 years to complete. Some patients were in the study for longer than 8 months because they took the medicine as long as they were having clinical benefit from the study medicine.

The sponsor ran this study at 10 locations in 2 countries, in Japan and the United States. It began 06 October 2014 and ended 31 October 2018. 13 men and 8 women participated. All patients were between the ages of 58 and 83 years.

Patients were supposed to be treated with glasdegib for at least 6 months. Of the 21 patients who started the study, 4 finished the 6 months of treatment with glasdegib. 17 patients did not finish the study. 1 patient died before finishing the study due to progression of their disease. 12 patients did not finish the study because they discontinued due to a medical problem they experienced. 4 patients left before

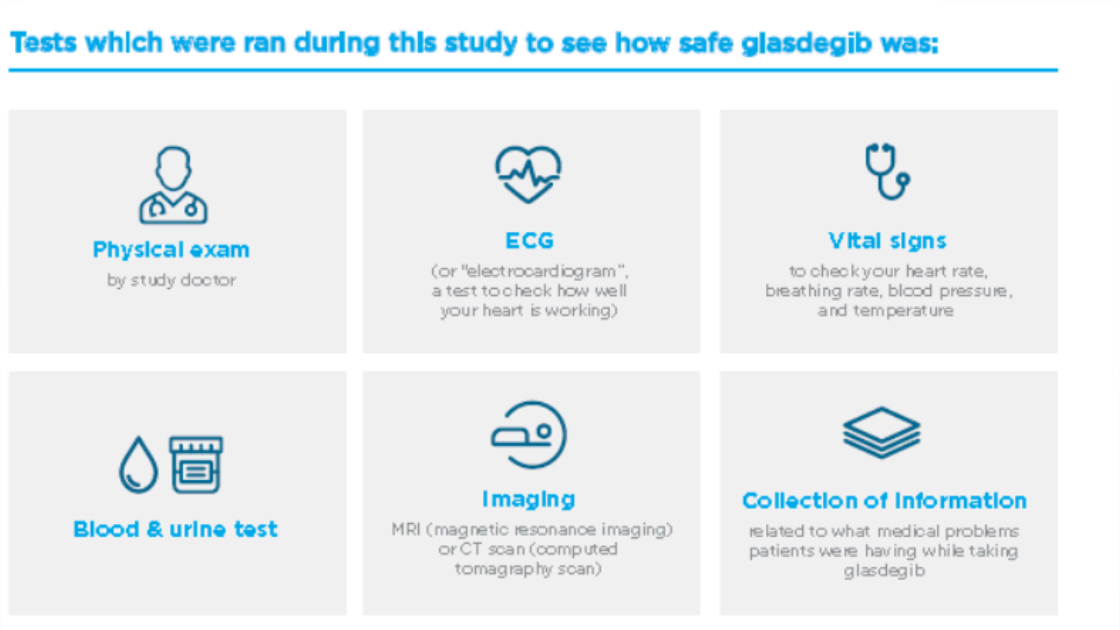
the study was over by their choice or a doctor decided it was best for a patient to stop the study.

When the study ended in October 2018, the Sponsor reviewed 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?

Was taking glasdegib safe for patients with myelofibrosis?

Patients were given a variety of different tests to see how safe glasdegib was. These included physical exams by doctors, ECGs (a test to see how well your heart is working), collection of information (such as medical problems the patient was experiencing during the study), vital signs, blood and urine tests, and imaging tests. See below picture for a summary of the tests ran during this study.

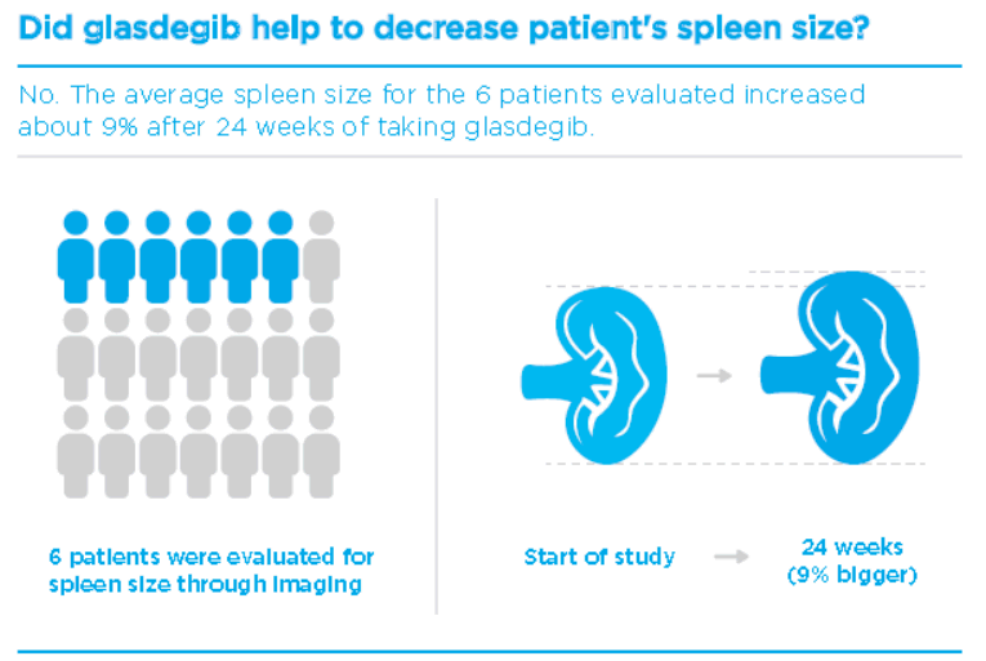


Based on the data collected from these tests, taking 100 mg of glasdegib daily per mouth was manageable for patients with MF. Also, taking glasdegib for longer periods of time did not appear to increase medical problems experienced in these patients.

Did glasdegib help to decrease patient's spleen volume?

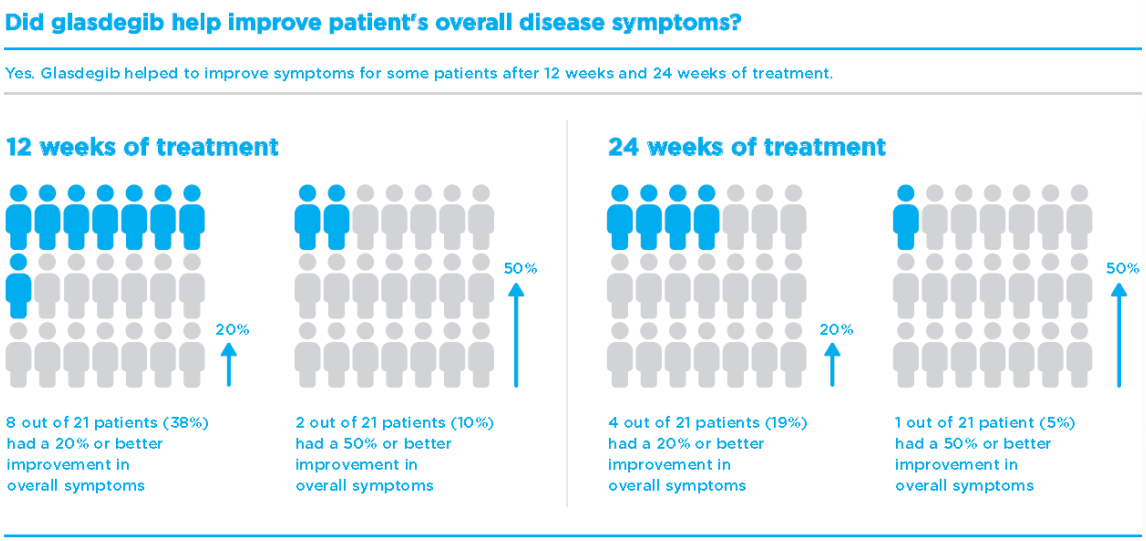
MF causes patients to have enlarged spleens. Researchers wanted to see if glasdegib could help reduce spleen volume.

5 patients did experience some reduction in spleen volume at some point in this study. However, after 24 weeks of treatment, the average spleen volume increased. 6 out of 21 patients were checked for spleen volume at the 24-week visit. There was an average increase of about 9% after taking glasdegib for 24 weeks.



Did glasdegib help to improve patient's overall disease symptoms?

Patients took surveys at each of the study visits to record what their symptoms of MF were and the severity of their symptoms. From this survey, researchers assigned them a total symptom score (TSS). Researchers wanted to see if patient's TSS improved after taking glasdegib. Researchers also wanted to see how many patient's TSS' improved at least 50% after taking glasdegib at the Week 24 visit. A summary of the results are shown in the below picture.



After 12 weeks of treatment with glasdegib:

- 8 out of 21 patients (or 38%) had a 20% or better improvement in symptoms.
- 2 out of 21 patients (or 10%) had a 50% or better improvement in symptoms.

After 24 weeks of treatment with glasdegib:

- 4 out of 21 patients (or 19%) had a 20% or better improvement in symptoms.
- 1 out of the 21 patients (or 5%) had a 50% or better improvement in symptoms.

Researchers concluded that based on these results that glasdegib may help improve patient's symptoms for patients with MF previously treated with ruxolitinib. 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 PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the participants reported 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.

All patients in this study had at least 1 non-serious medical problem. A "non-serious" medical problem is one that is not life-threatening, or does not cause lasting medical problems or death. A total of 12 patients (57%, or 12 out of 21 patients) left the study because of medical problems.

The most commonly reported medical problems were changes in how things tasted, muscle spasms, and loss of hair. The medical problems experienced by patients did not lead to any new safety concerns for glasdegib in patients with MF who had previously taken ruxolitinib.

The table below shows a list of the medical problems experienced by more than 5% of all patients (or at least 2 out of the 21 patients who participated in the study).

Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)	
Medical Problem	**Glasdegib (21 Patients Treated)**
Change or loss of taste	**13 (62%)**
Muscle cramps	**12 (57%)**
Loss of hair	**8 (38%)**
Decreased appetite	**7 (33%)**

Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)	
Medical Problem	**Glasdegib (21 Patients Treated)**
Fatigue	7 (33%)
Weight loss	6 (29%)
Low red blood cell count (low hemoglobin)	5 (24%)
High lipase in the blood (may indicate a problem with the pancreas)	5 (24%)
Nausea	4 (19%)
Fever	4 (19%)
High uric acid in the blood (may indicate a problem with the kidneys)	4 (19%)
Low platelet count (which can cause bleeding)	3 (14%)
Constipation	3 (14%)
Weakness	3 (14%)
Upper respiratory tract infection	3 (14%)
Abnormal electrical activity of the heart	3 (14%)
Low lymphocyte count (a type of white blood cell)	3 (14%)
Dehydration	3 (14%)
Muscle pain	3 (14%)
Pain in hands, arms, legs, or feet	3 (14%)
Dizziness	3 (14%)
Cough	3 (14%)
Rash	3 (14%)

Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)	
Medical Problem	**Glasdegib (21 Patients Treated)**
Low neutrophil count (a type of white blood cell)	2 (10%)
Abdominal pain	2 (10%)
Abdominal pain (upper pain only)	2 (10%)
Diarrhea	2 (10%)
Dry mouth	2 (10%)
Fall	2 (10%)
High blood sugar	2 (10%)
Back pain	2 (10%)
Difficulty breathing during exercise	2 (10%)
Night sweats	2 (10%)
Itchiness	2 (10%)
Itchiness all over the body	2 (10%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

5 patients (24%, or 5 out of 21 patients) had a total of 15 serious medical problems.
No type of serious medical problem was experienced by more than 1 patient.
1 patient had the same serious medical problem twice (respiratory failure).

Serious Medical Problems Experienced After Treatment with Glasdegib (Each Listed Problem Experienced by 1 Patient)	
• Fast heart rate	• Memory impairment
• Bleeding in the stomach veins	• Failure to thrive
• Enlarged veins in the esophagus	• Absence of bowel movement for 5 days after surgery
• Disease progression	• Confusion
• Fatigue	• Mental status changes
• Increase in the blood pressure within a system of veins in the liver called the portal venous system (Portal hypertension)	• Low oxygen in the body
• Bronchitis	• Respiratory failure

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.

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

www.clinicaltrials.gov	Use the study identifier **NCT02226172**
www.clinicaltrialsregister.eu	Use the study identifiers **2014-000933-21 and 2014-001048-40**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B1371013**

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!