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(s) Studied: Glasdegib (PF-04449913)

Protocol Number: B1371019

Dates of Study: 17 May 2021 to 02 December 2022

Title of this Study: Continuation Study of Azacitidine with or without Glasdegib in Patients With Untreated Acute Myeloid Leukemia, Myelodysplastic Syndrome or Chronic Myelomonocytic Leukemia

[A Multi-Center Continuation Study Evaluating Azacitidine With or Without Glasdegib (PF-04449913) in Patients With Previously Untreated Acute Myeloid Leukemia, Myelodysplastic Syndrome or Chronic Myelomonocytic Leukemia]

Date(s) of this Report: 22 December 2023

– 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 acute myeloid leukemia?

Acute myeloid leukemia is also known as AML and is a common cancer of the blood. AML starts when myeloid cells in the bone marrow begin to grow out of control. The bone marrow is the soft inner part of certain bones, and it is where new blood cells are made. The myeloid cells would normally develop into red blood cells, certain types of white blood cells, and platelets. Red blood cells are used to carry oxygen from the lungs around the body to where it is needed. These red blood cells also take carbon dioxide back to the lungs so it can be breathed out. White blood cells are used to fight infections. Platelets help to stop bleeding when blood vessels are damaged. While AML starts in the bone marrow, it often spreads to other areas of the body.

What is glasdegib?

This study investigated the use of glasdegib, which is a new type of treatment known as a hedgehog or smoothened inhibitors (hedgehog pathway plays a role in some cancer growth and hence, blocking this pathway may control the cancer growth). Glasdegib is designed to reduce or stop the growth of cancer cells. At the time this study began, glasdegib was an investigational (or experimental) drug. An investigational drug is one that is not approved for sale in the country where it is being used. During this study, the United States Food and Drug Administration gave their approval for glasdegib to be used with low dose cytarabine to treat newly diagnosed AML. This was in November 2018. The European Medicines Agency (EMA) gave their approval in June 2020. Glasdegib is sold in these countries as DAURISMO®.

The other treatment used in this study is azacitidine. Azacitidine is one of the licensed cancer treatments for AML and is often described as chemotherapy.

What was the purpose of this study?

- The purpose of the parent study was to compare the effects of the study drug, glasdegib, with a placebo, to find out how well glasdegib worked in combination with azacitidine (chemotherapy) to help participants live longer. Azacitidine is one of the medicines used to treat patients with AML in the US and Europe if the patient is not suitable for other choices of therapy.
- The main purpose of this continuation study was to find out how safe was the study drug glasdegib plus azacitidine (standard chemotherapy) treatment in participants, when compared to treatment with placebo plus azacitidine. This continuation study was an open label study. Open label means doctors and participants knew what study medication each patient was receiving. Continuation study means that it took place after another study with the same participants ended.

Researchers wanted to know:

- **What medical problems did participants have during the study?**
- **Did study participants have any serious medical problems during the study?**

What happened during the study?

How was the study done?

The parent study included participants with AML who had not previously been treated for their cancer. The participants were split into 2 groups:

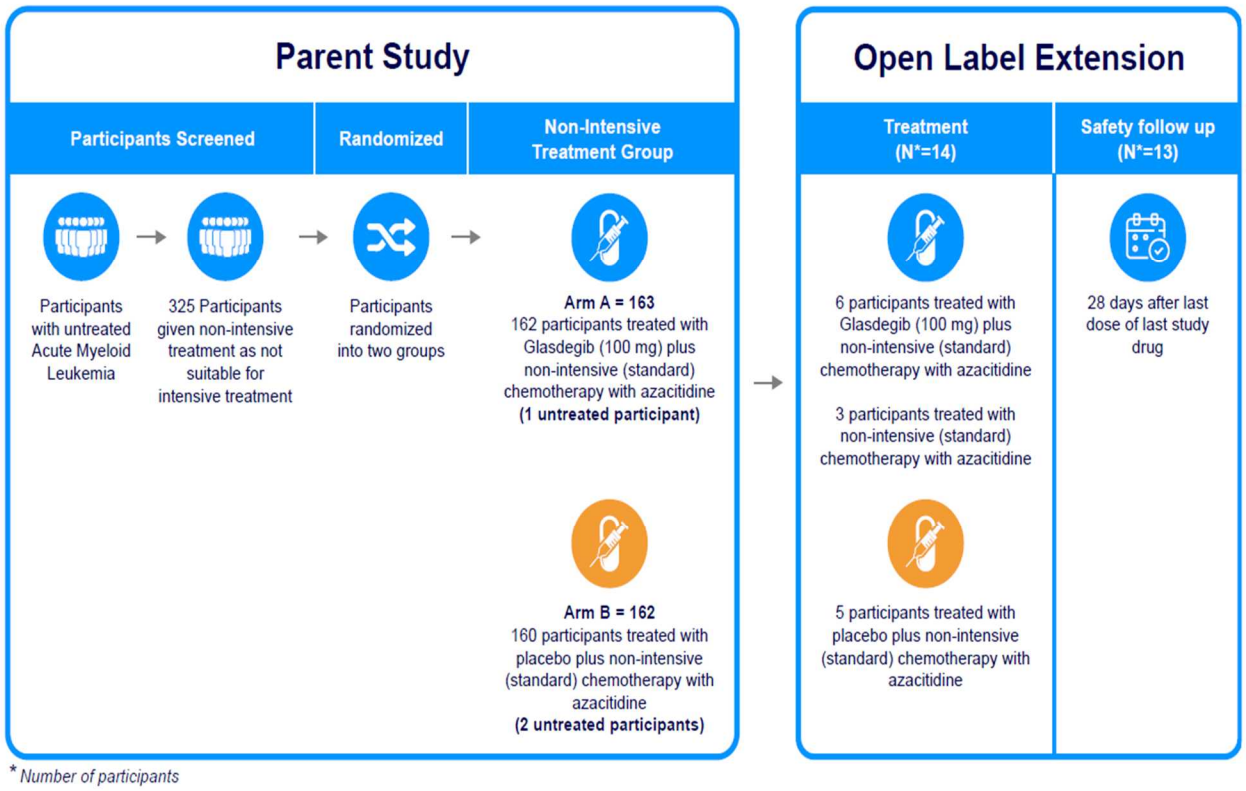
- An Intensive Treatment Group – included participants who were suitable for intensive chemotherapy with cytarabine and daunorubicin. Participants from this group did not continue into this continuation study. All participants in this group completed their treatment by 11 November 2021.
- A Non-intensive Treatment Group – included participants who were not suitable for intensive chemotherapy and who were given non-intensive (standard) chemotherapy with azacitidine
    - Continuation Study – This study was a continuation of the non-intensive treatment group participants who continued to show improvement in their cancer condition.

The researchers wanted to find out if study participants taking glasdegib plus standard chemotherapy with azacitidine had any medical problems or side effects compared to study participants given placebo plus standard chemotherapy with azacitidine. A placebo does not have any medicine in it, but it looks just like the study medication. Participants took glasdegib + azacitidine or azacitidine only, once a day. This treatment could be continued for up to 19 months. All participants received non-intensive chemotherapy, and this was given according to the manufacturer's recommendations. Participants who stopped treatment in this study were followed to check on their health.

Researchers compared the results of study participants taking glasdegib plus azacitidine to the results of study participants taking placebo plus azacitidine.

The Non-intensive study plan and the continuation study plan is shown in Figure 1.

Figure 1: Non-intensive study and the continuation study plan



* *Number of participants*

Where did this study take place?

The Sponsor ran this study at 11 locations in 11 countries.

When did this study take place?

The continuation study began on 17 May 2021 and ended on 02 December 2022.

Who participated in this study?

The study included participants who continued to show improvement in their cancer condition (as decided by the study doctor) from the treatment with azacitidine with or without glasdegib in non-intensive treatment groups.

- A total of 8 men participated
- A total of 6 women participated
- All participants were between the ages of 66 and 83 years.

Participants were to be treated until their cancer got worse, they experienced unacceptable toxicity, they left the study, or the participant died.

A total of 14 participants entered this continuation study from the parent study.

- In the glasdegib and azacitidine group, 6 out of 9 (66.7%), participants received both the glasdegib plus azacitidine and 3 out of 9 (33.3%) participants received azacitidine only. Of the 6 participants who received both glasdegib plus azacitidine, 3 participants discontinued the glasdegib treatment due to medical problems not related to study drug, lack of effectiveness and worsening of disease (1 [11.1%] participant each), and 3 participants discontinued the glasdegib treatment due to other reasons.
- All 14 participants (9 participants in the glasdegib plus azacitidine group and 5 participants in the placebo plus azacitidine group) received the standard chemotherapy with azacitidine and all 14 participants discontinued azacitidine at end of study.

A total of 13 participants entered the safety follow-up phase.

- In the glasdegib plus azacitidine group, 3 out of 8 (37.5%) participants completed the follow-up, 1 out of 8 (12.5%) participants died, and 4 out of 8 (50.0%) participants discontinued the follow-up due to other reasons.
- In the placebo plus azacitidine group, 1 out of 5 (20.0%) participants completed the follow-up, and 4 out of 5 (80.0%) participants discontinued the follow-up due to other reasons.

How long did the study last?

Participants took part in this continuation study after having participated in the parent study. Study participants were in the study for 2 months. The entire study took approximately 19 months' time to complete.

The study completed as planned. When the study ended in December 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

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.

In the glasdegib plus azacitidine Group, 7 out of 9 (77.8%) participants in this study had at least 1 medical problem. One (1) out of 9 (11.1%) participants left the study because of medical problems.

In the placebo plus azacitidine group, 4 out of 5 (80.0%) participants in this study had at least 1 medical problem. One (1) out of 5 (20.0%) participants left the study because of medical problems. The most common medical problems – those reported by at least 20% in at least any/either group of 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 more than 20% of participants are listed.
- The **2nd** column tells how many of the participants taking glasdegib plus azacitidine reported each medical problem. Next to this number is the percentage of the participants taking glasdegib plus azacitidine who reported the medical problem.
- The **3rd** column tells how many of the participants taking placebo plus azacitidine reported each medical problem. Next to this number is the percentage of the participants taking placebo plus azacitidine who reported the medical problem.

Using these instructions, you can see that:

- 4 out of 9 (44.4%) participants taking glasdegib plus azacitidine reported low numbers of white blood cells in the blood).
- 2 out of 5 (40.0%) participants taking placebo plus azacitidine reported low numbers of white blood cells in the blood.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Glasdegib plus Standard Chemotherapy (9 Participants)	Placebo plus Standard Chemotherapy (5 Participants)
Low numbers of neutrophils, a type of white blood cell, in the blood (neutropenia)	4 out of 9 participants (44.4%)	2 out of 5 participants (40.0%)
Low numbers of neutrophils, a type of white blood cell, in the blood plus fever (febrile neutropenia)	1 out of 9 participants (11.1%)	1 out of 5 participants (20.0%)

Swelling of legs or hands (oedema peripheral)	-	1 out of 5 participants (20.0%)
Platelet count decreased (thrombocytopenia)	1 out of 9 participants (11.1%)	1 out of 5 participants (20.0%)
Back pain	-	1 out of 5 participants (20.0%)

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.

- In the glasdegib plus azacitidine group, 2 out of 9 (22.2%) participants had serious medical problems. One (1) out of 9 (11.1%) participants died due to a medical problem not related to study treatment.
- In the placebo plus azacitidine group, 1 out of 5 (20.0%) participants had serious medical problems which was related to the study drug. No participant 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 B1371019

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

www.clinicaltrials.gov	Use the study identifier **NCT04842604**
www.clinicaltrialsregister.eu	Use the study identifier **2017-002822-19**

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!