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 Studied: Gemtuzumab ozogamicin (MYLOTARG™)

Protocol Number: B1761031

Dates of Study: 03 July 2019 to 27 April 2021

Title of this Study: A study to assess the general safety and effect of gemtuzumab ozogamicin (MYLOTARG™) on the heart of patients with CD33-positive acute myeloid leukemia and to see how the drug moves through the body

[A single-arm, open-label, phase 4 study evaluating QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin (MYLOTARG™) as a single-agent regimen in patients with relapsed or refractory CD33-positive acute myeloid leukemia]

Date of this Report: 30 March 2022

– 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 CD33-positive acute myeloid leukemia?

Acute myeloid leukemia (or "AML") is a type of blood cancer. This cancer is caused by too many immature white blood cells being made in the bone marrow. This reduces the ability of the body to make normal blood cells such as white blood cells (that fight off infections), red blood cells (that deliver oxygen to muscles and organs), and platelets (that help blood clot).

In normal cells, CD33 is a protein that is involved in helping cells communicate and connect/bond to things. They are also involved in cell growth. Cancer cells may grow more quickly.

Participants in this study had CD33-postive AML, which means that they had the CD33 protein on the surface of their cancer cells. Their CD33-positive AML was either:

- Relapsed: This means that the patient had a response to their most recent cancer treatment, but the cancer came back.

Or

- Refractory: This means that the patient did not have any response to their most recent cancer treatment, or the disease got worse while receiving the most recent treatment.

What is gemtuzumab ozogamicin (MYLOTARG™)?

Gemtuzumab ozogamicin (GO) (MYLOTARG™) is an antibody that attaches to myeloid cells (a type of cell in the bone marrow and blood) that have the CD33 protein. Once attached to the cancer cells, the drug delivers a substance into the cells and causes the diseased cell to die.

At the time of this study GO is the only approved AML therapy that specifically targets the CD33 protein.

In the United States (US), GO is approved for treating adults and children 1 month and older who have been diagnosed with CD33-positive AML for the first time. It is also approved for treating relapsed or refractory CD33-positive AML in adults and children 2 years and older. Participants in this study had relapsed or refractory CD33-positive AML.

In the European Union, GO is approved (to be given in combination with some other anti-cancer medications) for treating participants 15 years and older, who have been diagnosed with CD33-positive AML for the first time and have not previously been treated for their AML.

The Food and Drug Administration (FDA) asked the researchers to do some additional tests to see whether GO has an effect on the heart function (described in next section).

What was the purpose of this study?

The main goal of this study was to see if taking GO has an effect on the heart function (specifically the "QT interval") of participants with AML.

In this study, researchers used an electrocardiogram (ECG) machine, to measure heart function. The QT interval is a measurement made on the ECG that measures the electrical activity for part of the heart function.

The researchers wanted to see if there were any changes in the QT interval after taking GO, compared to before taking GO. Specifically, researchers wanted to see if GO causes "QT prolongation". QT prolongation occurs when the heart takes longer to contract and relax. This can affect the heart rhythm (beating of the heart) and can lead to life-threatening heart rhythm disorder.

To make sure the comparisons were accurate, researchers adjusted or "corrected" the QT interval using a special formula. This is so QT interval values could be compared

for different heart rates. The corrected QT interval is called "QTc". In this study, the corrected QTc values used to described results is called "QTcF".

Researchers wanted to know:

Did the participants have a change in their heart function (measured by QT change) after taking GO, compared to before taking GO?

What happened during the study?

How was the study done?

Researchers tested GO on a group of study participants with CD33-positive AML to find out if study participants taking GO had a change in their heart function.

This was an "open-label" study, which means that the researchers and the participants knew what study medication they were receiving. Apart from GO, participants also received their normal medications to relieve their cancer symptoms. Participants were also given medicines to help reduce symptoms such as fever and chills, known as "infusion reactions", before receiving GO.

Before being included in the study, participants were "screened" to see if they qualify to be in the study. During screening, a bone marrow or blood samples was collected to see if participants had CD33 on their cancer cells.

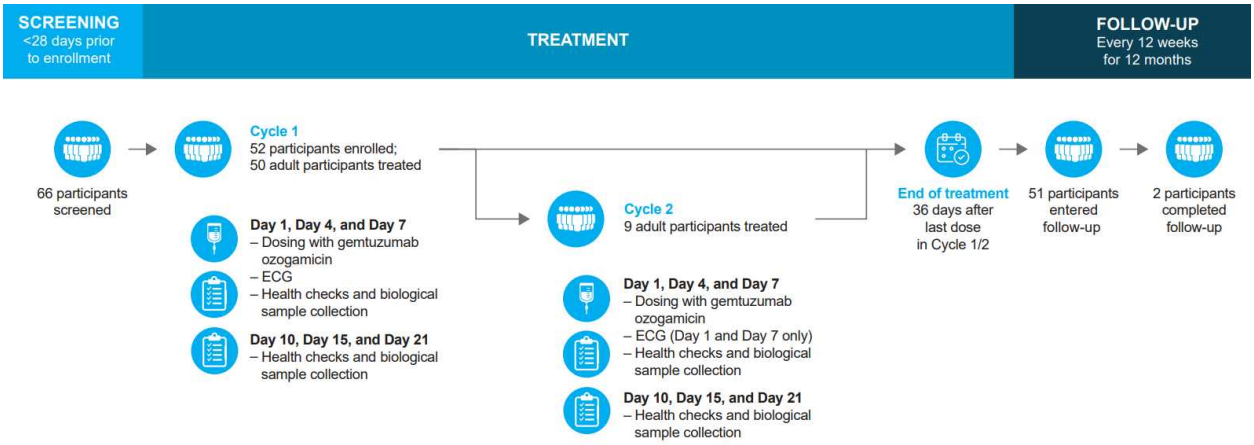
Participants were given 3 mg/m^2 of GO via intravenous (IV) infusion (using a "drip") on Days 1, 4 and 7 per cycle for 1 or 2 cycles. Infusion of the study medication took about 2 hours on each day. Some participants received GO for 1 cycle, and others for 2 cycles, depending on what the research doctors felt was best, and how what side effects the participants were having due to receiving GO.

Participants returned to the study unit for tests and biological sample collection on Days 10, 15 and 21 of each cycle, and had a final end-of-treatment (EoT) visit, 36 days after the last dose of GO, or start of new/other anticancer treatment.

After the EoT visit, participants were monitored every 12 weeks for 12 months, either via phone call or by being asked to return to the study unit for assessments, during a Follow-up Period.

Participants had regular ECGs to monitor changes in their heart. Participants also had other tests, and blood samples collected to monitor their safety, check the level of GO in their blood and how GO was processed by their body. Some participants also had urine samples collected. Participants were also asked about how well they were feeling, and about any other medications they were taking.

The schematic of the basic study plan is shown below.



Where did this study take place?

The Sponsor ran this study at 17 locations in 6 countries in Europe and North America.

When did this study take place?

It began on 03 July 2019 and ended on 27 April 2021.

Who participated in this study?

A total of 66 potential participants were screened to see if they qualify to be in the study.

In total, 52 participants (51 adults and 1 teenager) who had CD33-positive AML that was either relapsed or refractory, qualified to be in the study. Only results for the 51 adult participants are shown in this report.

Participants included in the study also met specific criteria with regards to the status of their leukemia, their heart rate measurements (specifically, QT interval), and their current and previous treatments for their cancer.

- A total of 31 men participated
- A total of 20 women participated
- All participants were between the ages of 22 years and 82 years.

Of the 51 adult participants in the study, 50 participants received at least 1 dose of study medication. One participant did not receive any treatment.

Of the 50 participants who received study medication:

- 46 of the 50 participants (92%) completed Cycle 1 treatment, and
- 9 of the 50 participants (18%) completed Cycle 2 treatment.

Two of the participants did not complete their assigned treatment due to medical problems.

All 51 participants (including the 1 participant who did not receive any study medication) entered the follow-up part of the study. Most of the participants (49 of

the 51 participants [96%]) did not complete the follow-up part of the study, due to the following reasons:

- Participant passed away: 45 of the 51 participants (88%)
- Participant decided they did not want to be in the study anymore: 2 of the 51 participants (4%)
- Researchers were unable to contact the participant: 1 of the 51 participants (2%)
- Other reason: 1 of the 51 participants (2%)

How long did the study last?

Study participants were in the study for about 12 months. The entire study took 1 year and 9 months to complete.

When the study ended in April 2021, 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 the participants have a change in their heart function (measured by QT change) after taking GO, compared to before taking GO?

Only results for all adult participants are shown below.

The study found that GO did cause changes in heart function, measured by QT change. None of the changes were of concern to researchers though.

Did the study medication cause QTc prolongation?

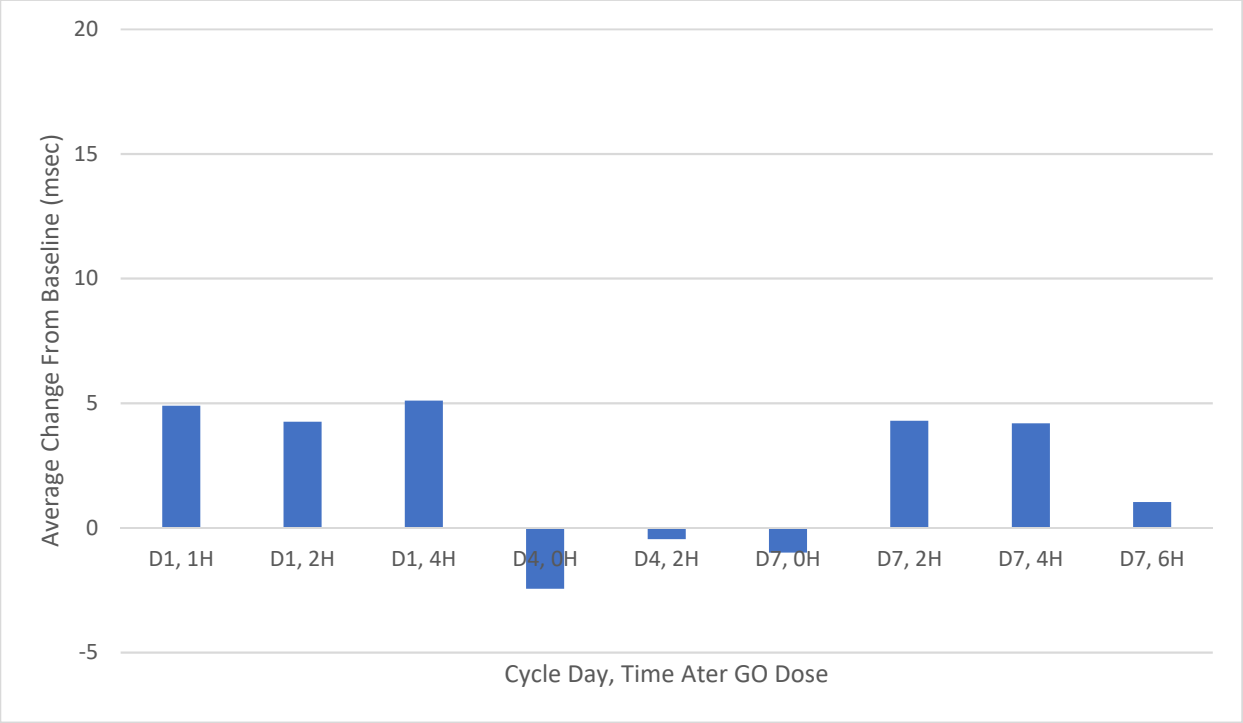
The researchers did a comparison ("analysis") of QTc interval values before taking GO and after taking GO using statistical tests. They used QTcF for the main comparison.

Figure 1 shows the average changes in QTc from before the first dose of GO was given ("baseline") to different time points in Cycle 1 after GO was given. Time points assessed were Day 1 (at 1, 2 and 4 hours), Day 4 (at 0 and 2 hours) and Day 7 (at 0, 2, 4 and 6 hours). Bars above the line show increases in QTcF from baseline, and bars below the line show decreases in QTcF from baseline.

Researchers decided beforehand on a specific cut off value that would tell them if the change in QTc was significant or not. The study found that the largest possible difference in QTc values after taking GO calculated by researchers was below the cut off value. This means that QTc values after taking GO were acceptable compared to average QTc values at baseline, for the time points in this study. The researchers did not think that GO causes significant QTc prolongation.

There were no participants with individual QTc changes from baseline or maximum QTc values that were of concern to researchers.

Figure 1. Summary of Average QTcF Change From Baseline in Cycle 1



D = Day; H = hours after first dose of GO on each dosing day

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 medication might have on a participant.

Only results for all adult participants are shown below.

Forty-nine (49) out of 50 participants (98%) in this study who received GO in the study had at least 1 medical problem. The most common medical problems – those reported by 10% or more 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 10% of participants are listed.
- The **2nd** column tells how many of the 50 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 50 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 20 out of the 50 participants (40%) taking the study medication had a medical problem of low white blood cells count with fever.

Some participants had medical problems related to their heart rate, but most were mild to moderate. One participant had medical problems of 'irregular heartbeat' and 'rapid heartbeat' that were considered severe.

No participants had side effects related to the electrical activity of their heart, that were considered life-threatening or caused the death of the participant.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**Study Medication (50 Participants)**
Low white blood cell count with fever	20 out of 50 participants (40%)
Low blood platelets	11 out of 50 participants (22%)
Low blood potassium	9 out of 50 participants (18%)
Fever	9 out of 50 participants (18%)
Nausea	8 out of 50 participants (16%)
Blood stream infection	7 out of 50 participants (14%)
Low red blood cell count	6 out of 50 participants (12%)
Vomiting	6 out of 50 participants (12%)
Increased liver enzymes in blood	5 out of 50 participants (10%)
Constipation	5 out of 50 participants (10%)
Diarrhea	5 out of 50 participants (10%)
AML got worse	5 out of 50 participants (10%)
Nosebleed	5 out of 50 participants (10%)
Headache	5 out of 50 participants (10%)
Low blood magnesium levels	5 out of 50 participants (10%)
Low levels of white blood cells	5 out of 50 participants (10%)

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.

A total of 34 out of 50 participants (68%) had serious medical problems. Serious medical problems that were reported for 2 or more participants are shown in **Table 2**.

Most of the serious medical problems were not considered by researchers to be related to GO. A total of 5 out of 50 participants (10%) had serious medical problems that researchers thought might be related to GO.

- Low white blood cell counts with fever in 3 out of 50 participants (6%)
- Low blood platelets in 1 out of 50 participants (2%)
- Bacterial infection of the kidneys, bladder or urethra in 1 out of 50 participants (2%)
- Blood vessel leakage in 1 out of 50 participants (2%)

Use the same for reading Table 2 as provided for Table 1.

Table 2. Serious medical problems reported by 2 or more participants in the study	
Serious Medical Problem	**Study Medication (50 Participants)**
Low white blood cell count with fever	11 out of 50 participants (22%)
Blood stream infection	7 out of 50 participants (14%)
AML got worse	5 out of 50 participants (10%)
Fever	3 out of 50 participants (6%)
Pneumonia	3 out of 50 participants (6%)
Non-typical pneumonia	2 out of 50 participants (4%)
Low blood platelets	2 out of 50 participants (4%)

Overall, 45 out of 50 (90%) participants passed away during the entire study (including the follow-up period), due to the following reasons:

- AML got worse ("disease progression"): 35 out of 50 participants (78%)
- Blood vessel leakage: 1 out of 50 participants (2%)
- Other reasons: 14 out of 50 participants (31%)

Only the event of "blood vessel leakage" was considered by the researchers to be potentially related to GO.

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 NCT03727750
www.clinicaltrialsregister.eu	Use the study identifier 2018-002619-89

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!