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: B1371012

Dates of Trial: 28 April 2015 to 29 January 2020

Title of this Trial: A Combination Study of PF-04449913 (Glasdegib) and Azacitidine In Untreated MDS, AML and CMML Patients (BRIGHT 1012)

[An Open-Label Phase 1b Study of PF-04449913 (Glasdegib) in Combination With Azacitidine in Patients With Previously Untreated Higher-Risk Myelodysplastic Syndrome, Acute Myeloid Leukemia, or Chronic Myelomonocytic Leukemia]

Date(s) of this Report: 31 August 2020

– 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?

Acute myeloid leukemia (or "AML"), myelodysplastic syndrome (or "MDS"), and chronic myelomonocytic leukemia (or "CMML") are types of blood cancers that usually affect patients over the age of 40. These cancers are 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).

The treatment options for AML, MDS, and CMML are limited if the patient can't receive "intensive" chemotherapy (strong medications) because of other medical problems. Researchers are looking for new medicines that can help patients with AML, MDS, and CMML live longer without their cancer rapidly getting worse.

Glasdegib (now approved under the brand name Daurismo® in the United States) was the investigational medicine tested in this study, and it was not yet approved at the beginning of this study. Glasdegib was developed to help reduce growth of cancerous stem cells in the bone marrow. Cancer stem cells are cells that self-regenerate and contribute to tumor growth. These cancer stem cells may be one of the reasons why some cancers return after chemotherapy treatment.

The main purpose of this study was to learn more about the use of glasdegib in patients with AML, MDS, and CMML, when given in combination with a chemotherapy medicine called azacitidine. Azacitidine is the standard treatment that is usually given for patients with AML, MDS, and CMML. This study was divided into 2 parts, or "phases". Researchers asked these questions:

- **Phase 1: What medical problems did patients have during treatment with glasdegib and azacitidine?**
- **Phase 2: How many patients would achieve "complete remission" when taking glasdegib and azacitidine?**

In this study, complete remission or complete response meant that the patients no longer had any evidence of AML, MDS, or CMML.

WHAT HAPPENED DURING THE STUDY?

This study included patients who:

- Were diagnosed with AML, or medium to high risk MDS or CMML, and had not received treatment for their AML, MDS, or CMML before
- Aged ≥18 years
- Had adequate liver and kidney function
- Were appropriate for treatment with azacitidine
- Able to walk around, take care of themselves, and be active for more than 50% of the day (Phase 1 only)
- Were not healthy enough to be treated with intensive chemotherapy (Phase 2 only)

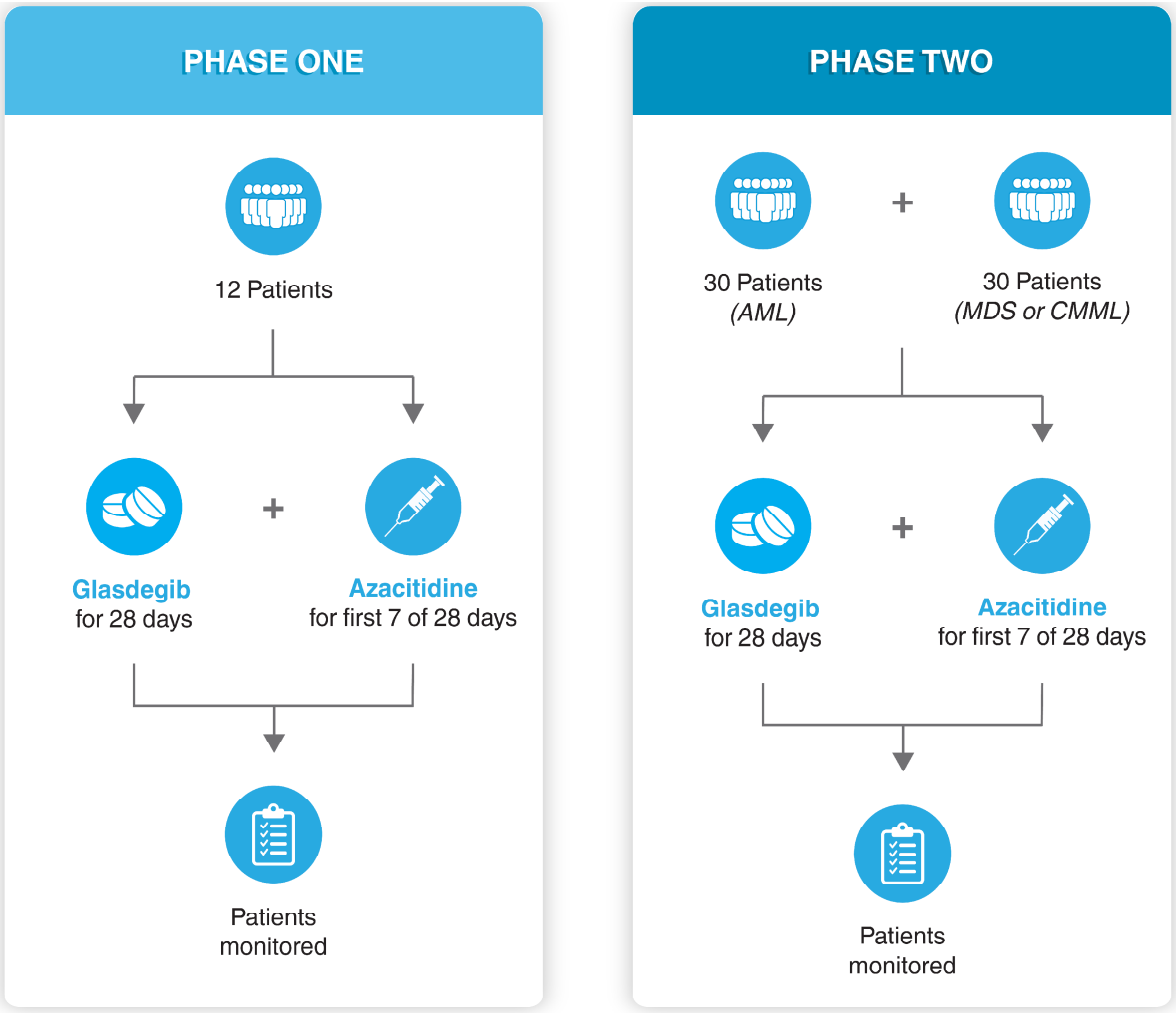
What happened during Phase 1 of the study?

During Phase 1 of this study, 12 patients received glasdegib in combination with azacitidine. The goal of Phase 1 was to learn more about the safety of glasdegib in combination with azacitidine. The starting dose of glasdegib was 100 mg in pill form, once daily by mouth for 28 days. The starting dose of azacitidine was 75 mg per square meter of body surface area, given as injections under the skin. Patients took azacitidine in cycles, which means that it was taken for only the first 7 days of each 28 days. The patients were monitored for medical problems.

What happened during Phase 2 of the study?

The goal of Phase 2 was to find out how many patients would achieve complete remission. 30 patients with MDS or CMML and 30 patients with AML received glasdegib in combination with azacitidine. The starting dose of glasdegib was 100 mg in pill form, once daily by mouth for 28 days. The starting dose of azacitidine was 75 mg per square meter of body surface area, given as injections under the skin or into the vein. Patients took azacitidine in cycles, which means that it was taken for only the first 7 days of each 28 days. Patients with MDS or CMML were monitored for at least 28 weeks, and patients with AML were monitored for at least 24 weeks.

The figure below shows what happened during the study.



The amount of time that patients were in the study varied depending on their response to study treatment, but the entire study took almost 5 years to complete. The Sponsor ran this study at 32 locations in 6 countries in North America and Europe. It began 28 April 2015 and ended 29 January 2020. A total of 5 women (42%) and 7 men (58%) participated in Phase 1, and 18 women (30%) and 42 men (70%) participated in Phase 2. All patients were between the ages of 55 and 89.

Patients were to be treated until their AML, MDS, or CMML stopped responding or got worse, until they developed unacceptable medical problems, or until they chose to stop treatment or started a new treatment for AML, MDS, or CCML. Of the 60 patients who started Phase 2 of the study, 21 were still in the study at the time of this report. A total of 39 patients left Phase 2 before the study was over by their choice, because a doctor decided it was best for a patient to stop being in the study, or because the patient died. This included 15 patients (50%) with MDS or CMML and

24 patients (80%) with AML. Patient death was the most common reason that patients left the study early.

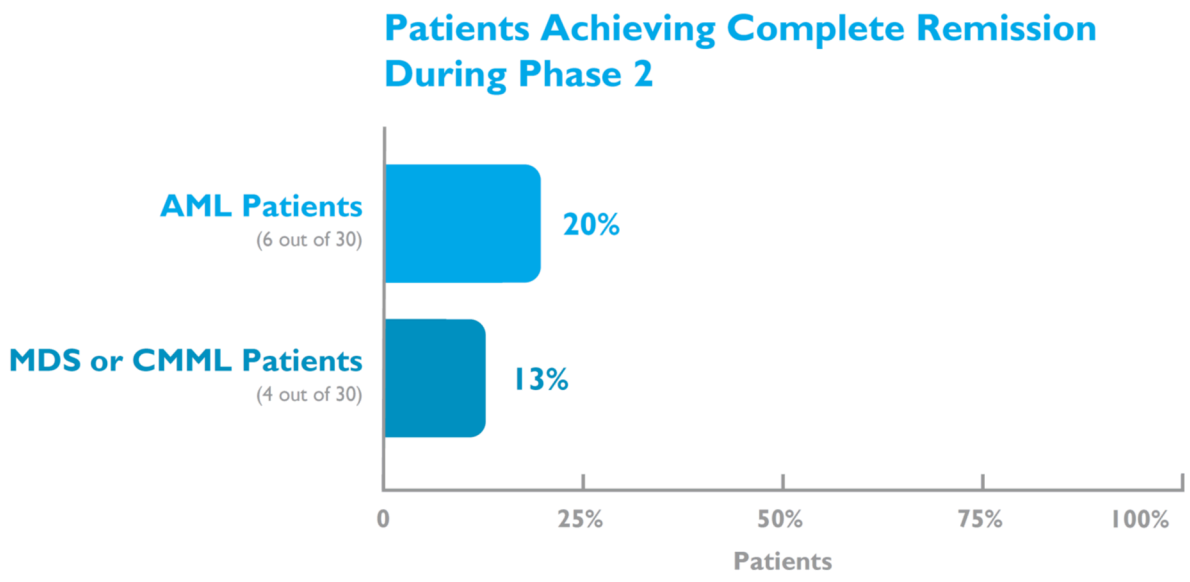
When the study ended in January 2020, the Sponsor reviewed the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

During Phase 2 of the study, how many patients achieved complete remission while taking glasdegib?

6 out of 30 patients with AML (20%) achieved complete remission during Phase 2. 4 out of 30 patients with MDS or CMML (13%) achieved complete remission during Phase 2. Based on these results, the researchers have decided that the results are not likely due to chance. The test medicine may be an option for treating patients with AML, MDS, or CMML.

These results are shown in the graph 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 PATIENTS HAVE DURING THE STUDY?

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.

During Phase 1, all patients in this study (100%) had at least 1 medical problem. A total of 6 patients (50%) left the study because of medical problems. Researchers also looked at how severe the medical problems were determined to be by the study doctors. The most common medical problems during Phase 1 are listed below, along with their severity.

Most Common Medical Problems and Severity in Phase 1 (Reported by More Than 30% of Patients)

Medical Problem	Mild	Moderate	Severe	Life-Threatening/ Disabling	Death Related to Medical Problem	Total With Medical Problem (12 Patients Treated)
Constipation	4 (33%)	5 (42%)	0 (0%)	0 (0%)	0 (0%)	9 (75%)
Low number of red blood cells	0 (0%)	0 (0%)	8 (67%)	1 (8%)	0 (0%)	9 (75%)
Nausea	2 (17%)	6 (50%)	0 (0%)	0 (0%)	0 (0%)	8 (67%)

Diarrhea	**4 (33%)**	**2 (17%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**6 (50%)**
Tiredness	**2 (17%)**	**3 (25%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**6 (50%)**
Low number of a type of white blood cells (neutrophils)	**0 (0%)**	**0 (0%)**	**1 (8%)**	**5 (42%)**	**0 (0%)**	**6 (50%)**
Change in sense of taste	**3 (25%)**	**2 (17%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**5 (42%)**
Weight loss	**2 (17%)**	**3 (25%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**5 (42%)**
Change in heart rhythm ("prolonged QT")	**1 (8%)**	**3 (25%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**5 (42%)**
Vomiting	**3 (25%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**
Runny nose	**4 (33%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**
Fever	**1 (8%)**	**2 (17%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**
Muscle spasms	**2 (17%)**	**1 (8%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**
Low number of a type of white blood cells (neutrophils) with fever	**0 (0%)**	**0 (0%)**	**4 (33%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**
Trouble breathing	**2 (17%)**	**1 (8%)**	**0 (0%)**	**1 (8%)**	**0 (0%)**	**4 (33%)**
Hair loss	**3 (25%)**	**1 (8%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**4 (33%)**

For Phase 1, the researchers also looked at how many medical problems were related to study treatment. All Phase 1 patients (100%) had medical problems that were considered to be related to study treatment by the study doctors. The most common related medical problems during Phase 1 are listed below, along with their severity.

Most Common Related Medical Problems and Severity in Phase 1 (Reported by More Than 30% of Patients)						
Medical Problem	Mild	Moderate	Severe	Life-Threatening/ Disabling	Death Related to Medical Problem	Total With Medical Problem (12 Patients Treated)
Nausea	2 (17%)	6 (50%)	0 (0%)	0 (0%)	0 (0%)	8 (67%)
Constipation	4 (33%)	3 (25%)	0 (0%)	0 (0%)	0 (0%)	7 (58%)
Low number of red blood cells	0 (0%)	0 (0%)	6 (50%)	0 (0%)	0 (0%)	6 (50%)
Tiredness	1 (8%)	3 (25%)	1 (8%)	0 (0%)	0 (0%)	5 (42%)
Change in sense of taste	3 (25%)	2 (17%)	0 (0%)	0 (0%)	0 (0%)	5 (42%)
Change in heart rhythm ("prolonged QT")	2 (17%)	2 (17%)	1 (8%)	0 (0%)	0 (0%)	5 (42%)
Low number of a type of white blood cells (neutrophils)	0 (0%)	0 (0%)	0 (0%)	4 (33%)	0 (0%)	4 (33%)
Weight loss	2 (17%)	2 (17%)	0 (0%)	0 (0%)	0 (0%)	4 (33%)
Vomiting	3 (25%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	4 (33%)
Low number of a type of white blood cells (neutrophils) with fever	0 (0%)	0 (0%)	4 (33%)	0 (0%)	0 (0%)	4 (33%)
Hair loss	3 (25%)	1 (8%)	0 (0%)	0 (0%)	0 (0%)	4 (33%)

During Phase 2, all of the patients (100%) had at least 1 medical problem. A total of 6 patients with AML (20%) and 3 patients with MDS or CMML (10%) left the study because of medical problems. The most common medical problems during Phase 2 are listed below.

Most Common Medical Problems During Phase 2 (Reported by More Than 30% of Patients in Either Group)		
Medical Problem	**AML Group (30 Patients Treated)**	**MDS/CMML Group (30 Patients Treated)**
Nausea	19 (63%)	20 (67%)
Constipation	18 (60%)	15 (50%)
Low appetite	17 (57%)	9 (30%)
Diarrhea	16 (53%)	14 (47%)
Vomiting	14 (47%)	10 (33%)
Fever	10 (33%)	5 (17%)
Muscle spasms	9 (30%)	15 (50%)
Tiredness	8 (27%)	9 (30%)
Low number of red blood cells	7 (23%)	12 (40%)
Low number of platelets in blood	5 (17%)	11 (37%)
Change in sense of taste	4 (13%)	13 (43%)
Low blood pressure	3 (10%)	9 (30%)
Low number of a type of white blood cell (neutrophil)	1 (3%)	11 (37%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

During Phase 1, 9 out of 12 patients (75%) had serious medical problems, including 7 patients (58%) with serious medical problems that were considered to be related to study treatment. The table below shows the most common serious medical problems during Phase 1, along with their severity.

Most Common Serious Medical Problems and Severity in Phase 1 (Reported by 2 or More Patients)

Serious Medical Problem	Mild	Moderate	Severe	Life-Threatening/ Disabling	Death Related to Medical Problem	Total With Serious Medical Problem (12 Patients Treated)
Low number of a type of white blood cells (neutrophils) with fever	0 (0%)	0 (0%)	4 (33%)	0 (0%)	0 (0%)	4 (33%)
Fever	0 (0%)	1 (8%)	1 (8%)	0 (0%)	0 (0%)	2 (17%)
Bacterial infection of skin and soft tissues	0 (0%)	1 (8%)	0 (0%)	1 (8%)	0 (0%)	2 (17%)

9 out of 12 patients (75%) passed away during Phase 1 of the study. Most deaths were due to the patient's AML, MDS, or CMML getting worse.

During Phase 2, 24 patients with AML (80%) had serious medical problems, including 8 patients (27%) with serious medical problems that were considered to be related to

study treatment. 18 patients with MDS or CMML (60%) had serious medical problems, including 8 patients (27%) with serious medical problems that were considered to be related to study treatment. The table below shows the most common serious medical problems during Phase 2.

Most Common Serious Medical Problems During Phase 2 (Reported by More Than 5% of Patients in Either Group)		
Serious Medical Problem	**AML Group (30 Patients Treated)**	**MDS/CMML Group (30 Patients Treated)**
Low number of a type of white blood cell (neutrophils) with fever	**6 (20%)**	**5 (17%)**
Serious illness caused by body's response to infection	**1 (3%)**	**5 (17%)**
Fever	**4 (13%)**	**2 (7%)**
AML, MDS, or CMML got worse	**3 (10%)**	**2 (7%)**
Heart rhythm changes ("QT prolongation")	**2 (7%)**	**0 (0%)**
Urinary tract infection	**2 (7%)**	**0 (0%)**

22 patients with AML (73%) and 15 patients with MDS or CMML (50%) passed away during Phase 2 of the study. Most deaths were due to the patient's AML, MDS, or CMML getting worse.

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 **NCT02367456**
www.clinicaltrialsregister.eu	Use the study identifier **2014-001345-24**

Clinical trials with glasdegib are ongoing, and further trials are planned.

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!