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 (Daurismo®)

Protocol Number: B1371003

Dates of Trial: 27 June 2012 to 04 March 2019

Title of this Trial: A Study To Test PF-04449913 (Glasdegib) With Intensive or Non-Intensive Chemotherapy In Patients With Acute Myeloid Leukemia or Myelodysplastic Syndrome

[A Phase 1b/2 Study to Evaluate the Safety and Efficacy of PF-04449913, an Oral Hedgehog Inhibitor, in Combination With Intensive Chemotherapy, Low Dose Ara-C or Decitabine in Patients With Acute Myeloid Leukemia or High-Risk Myelodysplastic Syndrome]

Date(s) of this Report: 17 April 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") and myelodysplastic syndrome (or "MDS") 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 and MDS 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 and MDS 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.

This study was divided into 2 parts, or "phases". The main purpose of the first phase of the study (Phase 1) was to determine the best dose of glasdegib to use in the second phase of the study (Phase 2). To do this, the researchers asked:

- **What dose-limiting toxicities, or "DLTs", did patients have during 1 treatment cycle with glasdegib?**

  DLTs are certain medical problems caused by taking glasdegib which require the patient to lower the dose or stop taking the medicine temporarily or permanently.

For Phase 2, there were 2 main questions that the researchers wanted to ask, depending on whether the patients were "Fit" (healthy enough to be treated with intensive chemotherapy) or "Unfit" (unable to be treated with intensive chemotherapy because of other medical problems):

- **How many Fit patients would achieve "complete remission" when taking glasdegib?**

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

- **Do Unfit patients taking glasdegib with non-intensive chemotherapy (low-dose Ara-C, or "LDAC") live longer than those taking LDAC alone?**

  In this study, Unfit patients received an alternative chemotherapy medicine (LDAC) that was approved for use in patients at the time.

WHAT HAPPENED DURING THE STUDY?

This study included patients who:

- Were newly diagnosed with AML or high-risk MDS, and had not received treatment for their AML before. Patients could have received treatment for their MDS before enrolling in the study.
- Aged ≥18 years (for all Phase 1 patients and Phase 2 Fit patients) or aged ≥55 years (for Phase 2 Unfit patients)
- Able to walk around, take care of themselves, and be active for more than 50% of the day

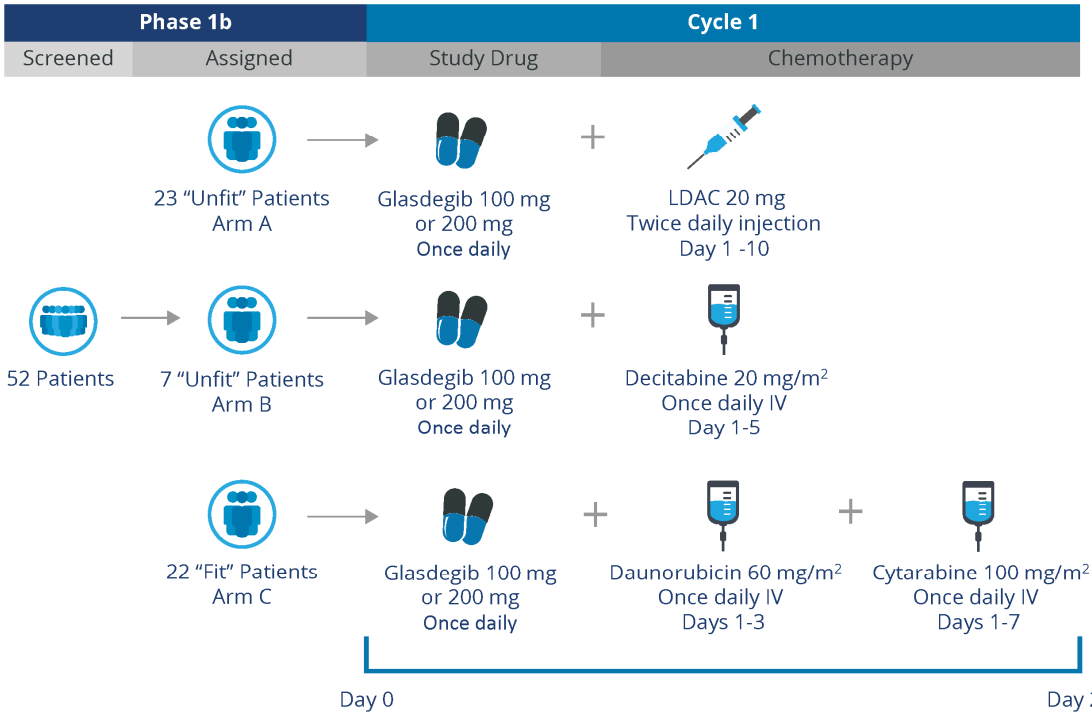
Patients were considered Unfit for intensive chemotherapy if they:

- Were aged ≥75 years, or
- Were unable to do any work (such as household chores), or
- Had evidence of kidney disease, or severe heart disease.

What happened during Phase 1 of the study?

Phase 1 of this study compared 3 groups of patients that were assigned to 1 of 2 doses of glasdegib (either 100 mg or 200 mg) to find the recommended dose of glasdegib for the Phase 2 portion of the study. The patients were also given chemotherapy treatment based on whether their doctor thought they were Fit or Unfit for intensive chemotherapy.

The figure on the next page shows what happened during Phase 1 of the study.

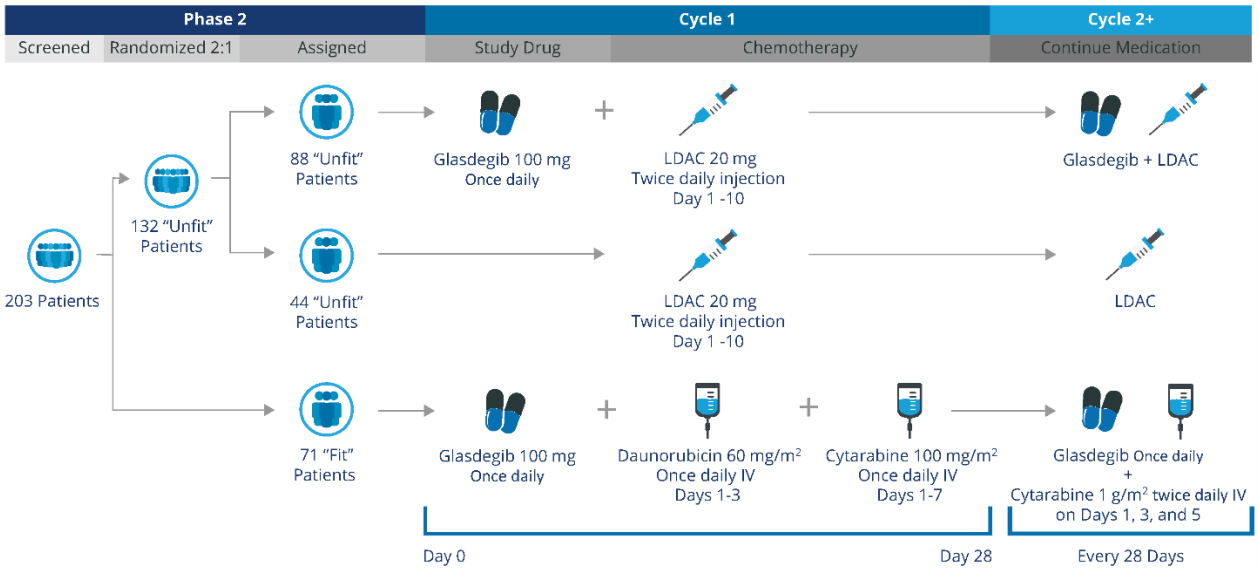


During Phase 1, each patient took 100 mg or 200 mg of glasdegib in pill form, once daily by mouth for 28 days. The patients were also treated with different chemotherapy drugs as shown above, and monitored for medical problems.

What happened during Phase 2 of the study?

Phase 2 of the study compared 2 groups of Unfit patients to find out if patients taking glasdegib with non-intensive chemotherapy (LDAC) would live longer than those taking LDAC alone. Unfit patients were assigned to each group by chance alone, which is known as a "randomized" study. This is done to make the groups more similar, which makes comparing the groups more fair. Twice as many patients were assigned to take glasdegib with LDAC, compared to LDAC alone. Phase 2 also treated 1 group of Fit patients, who took glasdegib along with intensive chemotherapy, to find out what percent would achieve complete remission.

The figure below shows what happened during Phase 2 of the study.



While most patients were only in the study for approximately 6 to 12 months, the entire study took over 6 years to complete. The Sponsor ran this study at 48 locations in 6 countries in North America and Europe. It began 27 June 2012 and ended 04 March 2019. A total of 20 women and 32 men participated in Phase 1, and 65 women and 138 men participated in Phase 2. All patients were between the ages of 27 and 92.

Patients were to be treated until their AML or MDS stopped responding or got worse, until they developed unacceptable medical problems, or until they chose to stop treatment. Of the 52 patients who started Phase 1 of the study, 9 finished the study. Of the 203 patients who started Phase 2 of the study, 23 finished the study. The most common reason for not completing the study was because the patient died. A total of 3 patients left Phase 1 and 8 patients left Phase 2 before the study was over by their choice or a doctor decided it was best for a patient to stop being in the study.

When the study ended in March 2019, 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 1 of the study, what dose-limiting toxicities (DLT) were reported?

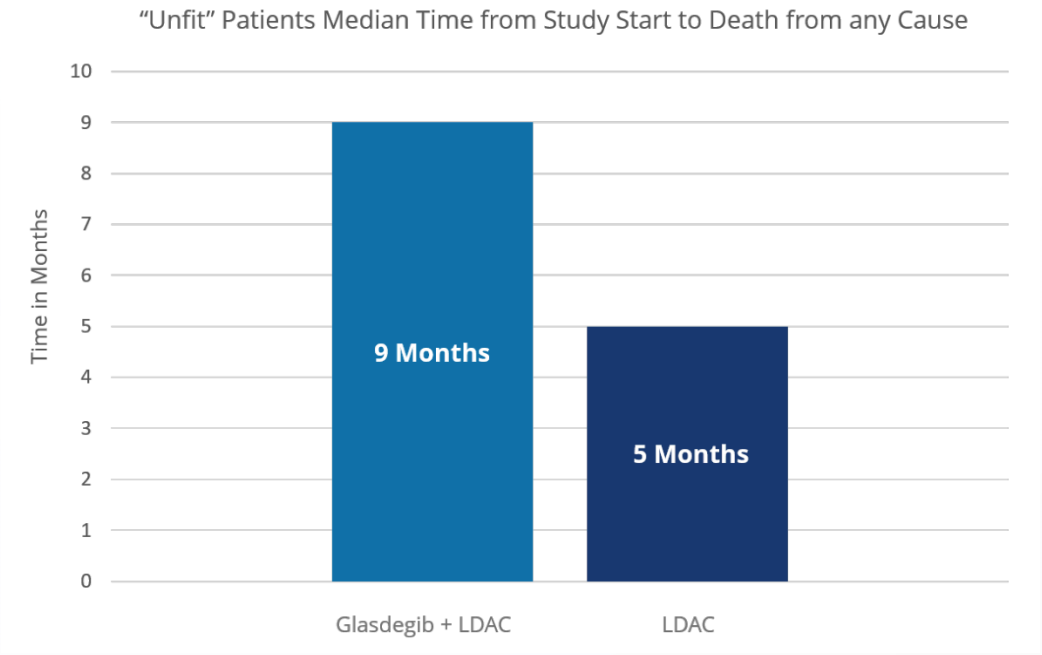
During Phase 1, researchers wanted to find the correct dose of glasdegib for treating patients with AML or MDS. To find the correct dose, the researchers needed to know how many patients in each dose group had a DLT during their first 28-day treatment cycle.

There was 1 patient who had a DLT. This patient was in the Fit group and took 100 mg of glasdegib once a day with intensive chemotherapy. However, some of the patients who took either 100 mg or 200 mg of glasdegib once a day had other medical problems that caused them to temporarily stop or lower their dose of glasdegib. Using this information, the researchers decided that 100 mg once a day was the correct glasdegib dose to use during Phase 2 of the study.

During Phase 2 of the study, did Unfit patients taking glasdegib with non-intensive chemotherapy (LDAC) live longer than those taking LDAC alone?

The results suggested that Unfit patients taking glasdegib with LDAC lived longer than Unfit patients taking LDAC alone. The researchers measured the "median time" between starting the study medicines and the patients dying of any cause. The median time was the time point where half (50%) of the patients taking glasdegib with LDAC, or LDAC alone, had passed away from any cause. Patients taking glasdegib with LDAC lived a median of 9 months from receiving their first dose of study medication until dying from any cause. Patients taking LDAC alone lived a median of 5 months from receiving their first dose of study medication until dying from any cause. 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 or MDS who are unable to be treated with intensive chemotherapy.

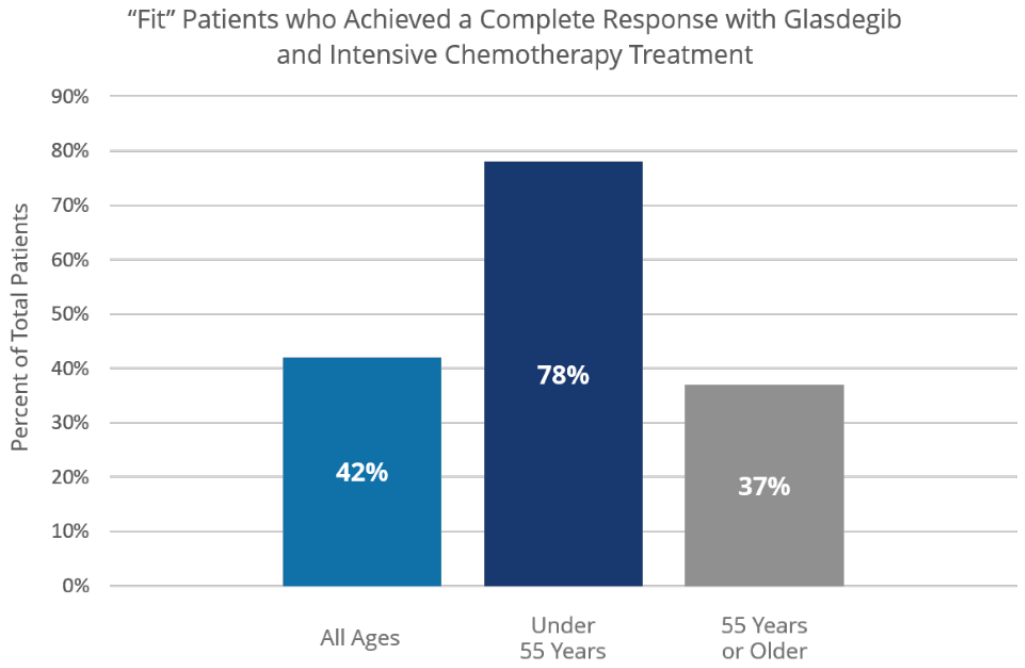
These results are shown in the graph on the next page.



During Phase 2 of the study, what percent of Fit patients achieved complete remission while taking glasdegib?

To answer this question, the researchers looked at the results for all patients, and then for patients who were under the age of 55 and patients who were 55 years of age or older. A total of 29 of 69 patients (42%) taking glasdegib with intensive chemotherapy achieved complete remission during the study. A total of 7 of 9 patients (78%) under the age of 55 and taking glasdegib with intensive chemotherapy achieved complete remission during the study. A total of 22 of 60 patients (37%) that were age 55 or older and taking glasdegib with intensive chemotherapy achieved complete remission during the study.

These results are shown in the graph on the next page.



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 had at least 1 medical problem. A total of 20 patients left the study because of medical problems. The most common medical problems during Phase 1 are listed below. To view the full list of medical problems reported by 5% or more of patients, please visit www.clinicaltrials.gov or www.clinicaltrialsregister.eu and use the study identifier information found at the end of this summary.

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

Medical Problem	Glasdegib 100 mg/200 mg + LDAC (23 Patients Treated)	Glasdegib 100 mg/200 mg + Decitabine (7 Patients Treated)	Glasdegib 100 mg/200 mg + Cytarabine/ Daunorubicin (22 Patients Treated)
Diarrhea	10 (44%)	2 (29%)	16 (73%)
Constipation	10 (44%)	3 (43%)	13 (59%)
Tiredness	8 (35%)	3 (43%)	8 (36%)
Low white blood cell count	7 (30%)	4 (57%)	5 (23%)
Low white blood cell count with fever	9 (39%)	1 (14%)	12 (55%)
Nausea	10 (44%)	5 (71%)	17 (77%)
Low blood platelets	7 (30%)	3 (43%)	5 (23%)
Muscle spasms	6 (26%)	2 (29%)	12 (55%)
Headache	4 (17%)	1 (14%)	11 (50%)
Fever	6 (26%)	1 (14%)	11 (50%)
Limb swelling	6 (26%)	1 (14%)	9 (41%)
Vomiting	3 (13%)	2 (29%)	9 (41%)
Bad taste in mouth	8 (35%)	2 (29%)	8 (36%)
Low blood potassium	5 (22%)	1 (14%)	8 (36%)
Low blood calcium	2 (9%)	1 (14%)	7 (32%)
Arm or leg pain	1 (4%)	2 (29%)	7 (32%)
Back pain	3 (13%)	4 (57%)	5 (23%)

Hair loss	2 (9%)	3 (43%)	6 (27%)
Low red blood cell count	4 (17%)	3 (43%)	5 (23%)
Loss of strength or energy	4 (17%)	3 (43%)	1 (5%)
Low appetite	3 (13%)	3 (43%)	4 (18%)

During Phase 2, all of the patients in this study had at least 1 medical problem. A total of 65 patients left the study because of medical problems. The most common medical problems during Phase 2 are listed below. To view the full list of medical problems reported by 5% or more of patients, please visit www.clinicaltrials.gov or www.clinicaltrialsregister.eu and use the study identifier information found at the end of this summary.

Most Common Medical Problems in Phase 2 (Reported by More Than 30% of Patients in Any Group)

	Phase 2 "Unfit"		Phase 2 "Fit"
Medical Problem	Glasdegib 100 mg + LDAC (84 Patients Treated)	LDAC (41 Patients Treated)	Glasdegib 100 mg + Cytarabine/ Daunorubicin (69 Patients Treated)
Diarrhea	24 (29%)	9 (22%)	49 (71%)
Low white blood cell count with fever	30 (36%)	10 (24%)	44 (64%)
Nausea	30 (36%)	5 (12%)	40 (58%)
Low blood potassium	13 (16%)	6 (15%)	37 (54%)
Fever	25 (30%)	9 (22%)	34 (49%)
Constipation	21 (25%)	6 (15%)	32 (46%)
Low red blood cell	38 (45%)	17 (42%)	28 (41%)

count			
Low appetite	**29 (35%)**	**5 (12%)**	**26 (38%)**
Tiredness	**27 (32%)**	**8 (20%)**	**25 (36%)**
Vomiting	**18 (21%)**	**4 (10%)**	**25 (36%)**
Low blood sodium	**11 (13%)**	**0**	**24 (35%)**
Low blood platelets	**26 (31%)**	**11 (27%)**	**23 (33%)**
Abdominal pain	**15 (18%)**	**4 (10%)**	**22 (32%)**
Headache	**11 (13%)**	**5 (12%)**	**22 (32%)**
Low blood calcium	**5 (6%)**	**1 (2%)**	**22 (32%)**
Limb swelling	**22 (26%)**	**7 (17%)**	**22 (32%)**

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, 37 patients (71%, or 37 out of 52 patients) had serious medical problems. Thirty-nine (39) patients passed away during Phase 1 of the study. Most deaths were due to the patient's AML or MDS getting worse.

During Phase 2, 135 patients (70%, or 135 out of 194 patients) had serious medical problems. In the Fit group, 35 patients had serious medical problems. In the Unfit groups, 68 patients receiving glasdegib and LDAC had serious medical problems, compared to 32 patients receiving only LDAC. A total of 162 patients passed away during Phase 2 of the study. Most deaths were due to the patient's AML or MDS getting worse.

Serious Medical Problems in Phase 1 (Reported by More Than 1 Patient in Any Group)

Medical Problem	Glasdegib 100 mg/200 mg + LDAC (23 Patients Treated)	Glasdegib 100 mg/200 mg + Decitabine (7 Patients Treated)	Glasdegib 100 mg/200 mg + Cytarabine/ Daunorubicin (22 Patients Treated)
Low white blood cell count with fever	6 (26%)	1 (14%)	2 (9%)
AML or MDS got worse	4 (17%)	1 (14%)	1 (5%)
Pneumonia	2 (9%)	2 (29%)	0
Infection of stomach or intestines	0	0	2 (9%)
Fell down	2 (9%)	0	0

Serious Medical Problems in Phase 2 (Reported by More Than 5% of Patients in Any Group)

	Phase 2 "Unfit"		Phase 2 "Fit"
Medical Problem	Glasdegib 100 mg + LDAC (84 Patients Treated)	LDAC (41 Patients Treated)	Glasdegib 100 mg + Cytarabine/ Daunorubicin (69 Patients Treated)
Low white blood cell count with fever	24 (29%)	7 (17%)	14 (20%)
Blood stream infection (sepsis)	3 (4%)	5 (12%)	6 (9%)
Pneumonia	19 (23%)	7 (17%)	4 (6%)
AML or MDS got worse	10 (12%)	5 (12%)	2 (3%)
Low red blood cell count	6 (7%)	0	0

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 **NCT01546038**
www.clinicaltrialsregister.eu	Use the study identifier **2012-000684-24**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B1371003**

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!