Summary of Results for Laypersons

Astellas is grateful to the patients who took part in this clinical study. Thank you.

What was the Study Called?

A Phase 1/2 Open-Label, Dose Escalation Study Investigating the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ASP2215 in Patients with Relapsed or Refractory Acute Myeloid Leukemia

Why was this Study Needed?

Acute myeloid leukemia (AML) is a type of cancer when bone marrow makes white blood cells that are not normal. These are called leukemia cells. Some patients with AML have a mutation or change in the FLT3 gene. This gene helps leukemia cells make a protein called FLT3. This protein causes the leukemia cells to grow faster. Relapsed AML means the cancer came back after it had disappeared with prior therapy. Refractory AML means the patients AML did not go away with a prior treatment such as chemotherapy, which is a cancer treatment that uses drugs to destroy cancer cells. Gilteritinib (also known as ASP2215) is a medicine taken by mouth. It is designed to slow down the growth of cancer cells by blocking proteins that stimulate production of cancer cells. When these proteins are blocked, they can no longer help cancer cells grow or survive.

This study was conducted in patients with AML whose cancer disappeared after prior treatment but then came back after that treatment stopped. Or whose cancer did not respond to prior treatment.

The question this study helped answer was what was the highest dose of gilteritinib that patients could tolerate. The study also looked at what the total amount of gilteritinib was in the patient's blood over time. And it measured the time it took for gilteritinib in the blood to decline by half.

It was also important to find out what unwanted effects the patients had from taking gilteritinib.

The study started in October 2013. The study ended in March 2018. When the study ended, Astellas reviewed all the study information and created a report of the results. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This was an "open-label" study. This means that all patients and the study doctors knew the patients took gilteritinib. The study included men and women 18 years of age and older with acute AML (either with or without a cancer causing change in the FLT3 gene). The patient's cancer either did not get better after earlier treatment. Or the cancer returned again after it had disappeared with the earlier treatment. Before starting this study, a sufficient amount of time was required between the prior treatment the patient received for their cancer and this new treatment with gilteritinib. They were active or they could perform light daily activities.

Or they were able to walk and capable of all self-care, but unable to carry out any work activities. And they were up and about more than half of the time that they were awake. Their liver, kidney, and heart worked sufficiently for the patient to enter the study.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study received one of the following gradually increasing doses of gilteritinib, by chance and the study doctor looked for unwanted effects with each dose.

- Gilteritinib 20, 40, 80, 120, 200, 300 or 450 mg tablets once a day by mouth during a period of time, called a cycle. A cycle in this study was 28 days.

Some patients took gilteritinib plus one of the following drugs. These drugs could affect how gilteritinib was taken up or broken down by the body. Or gilteritinib could affect that drug's removal from the body.

- Gilteritinib 20 mg with voriconazole 200 mg every 6 hours by mouth for 14 days in cycle 1
- Gilteritinib 300 mg with midazolam 2 mg by mouth on 2 days in cycle 1
- Gilteritinib 200 mg with cephalexin 500 mg by mouth on 2 days in cycle 1

The patients could take gilteritinib until their cancer got worse, they had unwanted effects they could not tolerate, they asked to stop treatment, or they enrolled in a follow-up study with gilteritinib.

This study took place at 27 clinics in 3 countries. 260 patients were in the study. Out of these patients, 252 patients took at least 1 dose of gilteritinib.

	Number of Patients
Age Group	
Aged less than 65 years	141
Aged 65 years or older	111
Sex	
Men	129
Women	123
Clinic Location	
USA	232
Italy	12
Germany	8

What Were the Study Results?

This study was done in patients with relapsed or refractory AML. The question this study helped answer was what the highest dose of gilteritinib was that patients could tolerate. The study also looked at what the total amount of gilteritinib was in the patient's blood over time. And it measured the time it took for gilteritinib in the blood to decline by half.

A 300 mg dose was the highest dose patients could tolerate. Patients received multiple doses of 120 mg gilteritinib. And the average total amount of gilteritinib in the blood over 24 hours

was 6180 ng·h/mL. ng·h/mL is a unit that measures the amount of gilteritinib in the blood over time. The time it took for the gilteritinib level in the body to decline by half was from 45 to 159 hours.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called "adverse events" and are recorded whether or not they might be caused by the treatment taken. An "adverse reaction" is any medical problem or "adverse event" that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

The table below shows the most common adverse reactions experienced by patients who took at least 1 dose of gilteritinib in this study.

Adverse Reaction	**Gilteritinib (out of 252 patients)**
Any adverse reaction	189 (75.0%)
Diarrhea	43 (17.1%)
Fatigue or tiredness	37 (14.7%)
Increased blood level of a liver enzyme (aspartate aminotransferase)	34 (13.5%)
Increased blood level of a liver enzyme (alanine aminotransferase)	29 (11.5%)
Increased blood level of an enzyme from muscles (creatine phosphokinase)	25 (9.9%)
Lack of enough red blood cells (anemia)	23 (9.1%)
Constipation	22 (8.7%)
Swelling of the ankles, feet or fingers	22 (8.7%)
Decreased number of a type of blood cell that helps to clot blood (platelet)	21 (8.3%)
Nausea or the urge to vomit	21 (8.3%)
Taste changes	19 (7.5%)
Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)	18 (7.1%)
Decreased level of blood platelets, which increases risk of bleeding or bruising	17 (6.7%)
Vomiting	17 (6.7%)
Abnormal electrical conduction within the heart	16 (6.3%)
Decreased appetite	14 (5.6%)
Decreased number of a type of white blood cell (neutrophil/granulocyte)	14 (5.6%)
Increased blood level of liver enzymes (transaminases)	14 (5.6%)
Decreased level of a type of white blood cell (neutrophils)	13 (5.2%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care.

In this study 30.2% or 76 out of 252 patients experienced serious adverse reactions: 2 patients who took 20 mg gilteritinib, 1 patient who took 40 mg gilteritinib, 10 patients who took 80 mg gilteritinib, 20 patients who took 120 mg gilteritinib, 37 patients who took 200 mg gilteritinib, 4 patients who took 300 mg gilteritinib, and 2 patients who took 450 mg gilteritinib.

215 patients died during the study. The deaths of 7 of the patients who took gilteritinib could have been related to gilteritinib.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of December 2018. You can find this summary and more information about this study online at http://www.astellasclinicalstudyresults.com.

Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. This summary only shows the results of this 1 study. Your doctor may help you understand more about the results of this study.

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