Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the effects of quizartinib in Japanese people with a type of blood cancer called relapsed or refractory acute myeloid leukemia

Protocol number: AC220-A-J201

Thank You!

Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for quizartinib. Each participant helped to advance medical research and knowledge for people affected with a type of blood cancer called relapsed or refractory acute myeloid leukemia. Their contribution to medicine and healthcare is greatly appreciated.

Important note: This summary only shows the results of a single study. Other studies may have different findings. Researchers and health authorities look at the results of many studies to understand which treatments work and how they work. It takes a lot of people in many studies around the world to advance medical science and healthcare.

Do not use the results of this study to make health decisions. Please talk to a doctor before changing any treatment you are taking or if you have any questions about these study results.

What was the main purpose of this study?

Acute myeloid leukemia (AML)

Researchers were looking for a better way to treat people with a type of blood cancer called relapsed or refractory acute myeloid leukemia, or AML. The participants in this study had AML that either:

- did not respond to all previous treatments (known as refractory AML) or
- responded but their disease came back again within 6 months of receiving their first treatment (known as relapsed AML).

AML is a cancer of the blood and the bone marrow. The bone marrow is found in the center of most bones, where new healthy blood cells are made. AML starts in the bone marrow and prevents it from making normal blood cells. The abnormal (cancer) cells build up in the bone marrow, so there are fewer healthy blood cells. These cancerous cells can also enter the blood stream and circulate in the blood, and go to different parts of the body.

The main treatment for AML is chemotherapy. Chemotherapy uses medicines to kill cancer cells or stop them from growing and dividing. You can have chemotherapy through a drip into a vein, as a tablet you swallow, or by an injection under the skin. People with AML might also have a procedure called a stem cell transplant, which attempts to remove the cancerous blood forming cells from the bone marrow and replace them with healthy cells taken, in most of the cases, from another healthy person (donor). The new cells can now multiply and produce healthy cells.

People with AML can have certain gene alterations (or mutations). People with FLT3-ITD positive AML have an alteration (or mutation) in the FLT3 gene. Participants in this study had FLT3-ITD AML. FLT3-ITD positive AML participants had severe symptoms, they did not respond well to standard treatment, and their AML was likely to come back even after treatment. Quizartinib is designed to work against AML cells with this genetic mutation. Researchers wanted to see how effective quizartinib is at treating Japanese patients with refractory or relapsed FLT3-ITD positive AML.

Treatment given in this study

Quizartinib

An investigational treatment that was being tested for the treatment of Japanese AML participants who were tested positive for FLT3-ITD.

Oral quizartinib was approved for use in Japan in June 2019.

Main purpose of this study

The main question the researchers wanted to answer in this study was:

How many AML participants showed composite complete remission to treatment with quizartinib?

Composite complete remission was defined as the sum of:

- **Complete remission,** which is also called **"CR"**: CR meant less than 5% of cells in the participants' bone marrow were cancer cells, with complete recovery of neutrophils and platelets*. There were no signs of AML in the bone marrow or any parts of the body, and the participants' blood cells had recovered without the need of any transfusion; plus
- **Complete remission with incomplete platelet recovery**, which is also called "**CRp": CRp** meant less than 5% of cells in the participants' bone marrow were cancer cells, with incomplete recovery of platelets; plus
- **Complete remission with incomplete hematological recovery**, which is also called "**CRi": CRi** means less than 5% of cells in their bone marrow were cancer cells, with incomplete recovery of neutrophils, with or without complete recovery of platelets. The participants may or may not have needed blood or platelet transfusion.

*Neutrophils are a type of white blood cells that fight bacteria. Platelets are a type of blood cells that help in preventing/stopping bleeding.

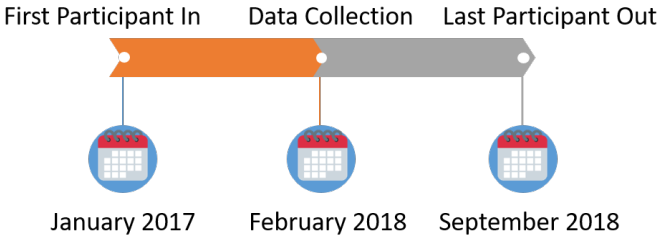
Other purposes of this study

Other questions researchers wanted to answer in this study were:

- How long did AML participants live after initiating treatment with quizartinib until they died due to any cause? This is also called 'Overall Survival'.
- How long did AML participants live until it was confirmed that the treatment did not benefit them, or their disease came back, or they died due to any cause? This is also called 'Event Free Survival'.
- What side effects did the participants develop during the study?

There were some additional questions that researchers wanted to answer but these are not discussed in this summary.

How long was this study?



This study was designed in such a way that the participants could continue in it as long as they did not meet certain criteria for discontinuing the treatment.

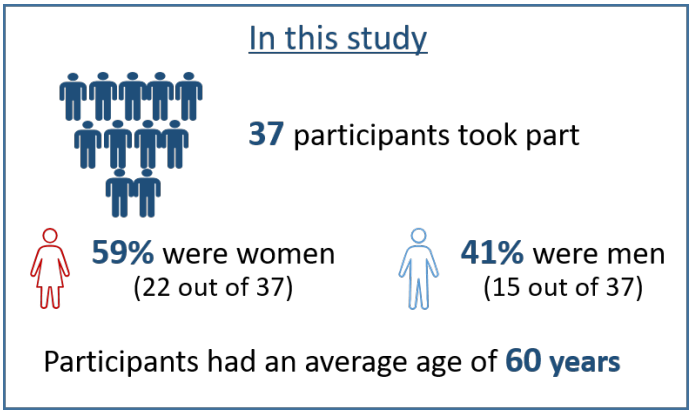
The first participant was enrolled in the study on 20 January 2017. The results were collected up to February 2018 for the study report. This summary is based on that report. The study completed as planned in September 2018.

Who was in this study?

This study included 37 participants from 34 sites in Japan.

Participants could take part in this study if they:

- were diagnosed with AML or had myelodysplastic syndrome (another type of blood cancer in which blood forming cells become abnormal) that progressed to AML,
- were Japanese and were 20 years and above,
- tested positive for the FLT3-ITD mutation,



- were previously treated for AML using standard intensive treatment,
- did not respond to their previous AML treatment, or did respond and were free of disease but only for less than 6 months and then their AML came back,
- did not have any major heart problems such as an irregular heart rhythm,
- were fully active, OR unable to do hard physical activity but able to walk and do light housework or office work, OR unable to work but able to walk and manage selfcare and be out of bed for more than 50% of waking hours, and
- did not have any other diseases or abnormal laboratory tests that could prevent them from attending study visits and assessments.

What happened during this study?

This was a Phase 2 study where treatment was given to a small number of participants with the disease condition to gather information about the effects of the study treatment in patients. This study was "open label". This means that both the researchers and the participants knew what treatment was given.

Participants were screened to find out if they could take part in the study. The starting dose of quizartinib was 20 or 30 milligram per day (mg/day), depending on the other medicines taken and whether they impacted the breakdown of quizartinib.

If the electrical activity in the heart of participants continued to be normal, the 20 mg/day dose could be increased to 30 mg/day, and the 30 mg/day dose could be increased to 60 mg/day.

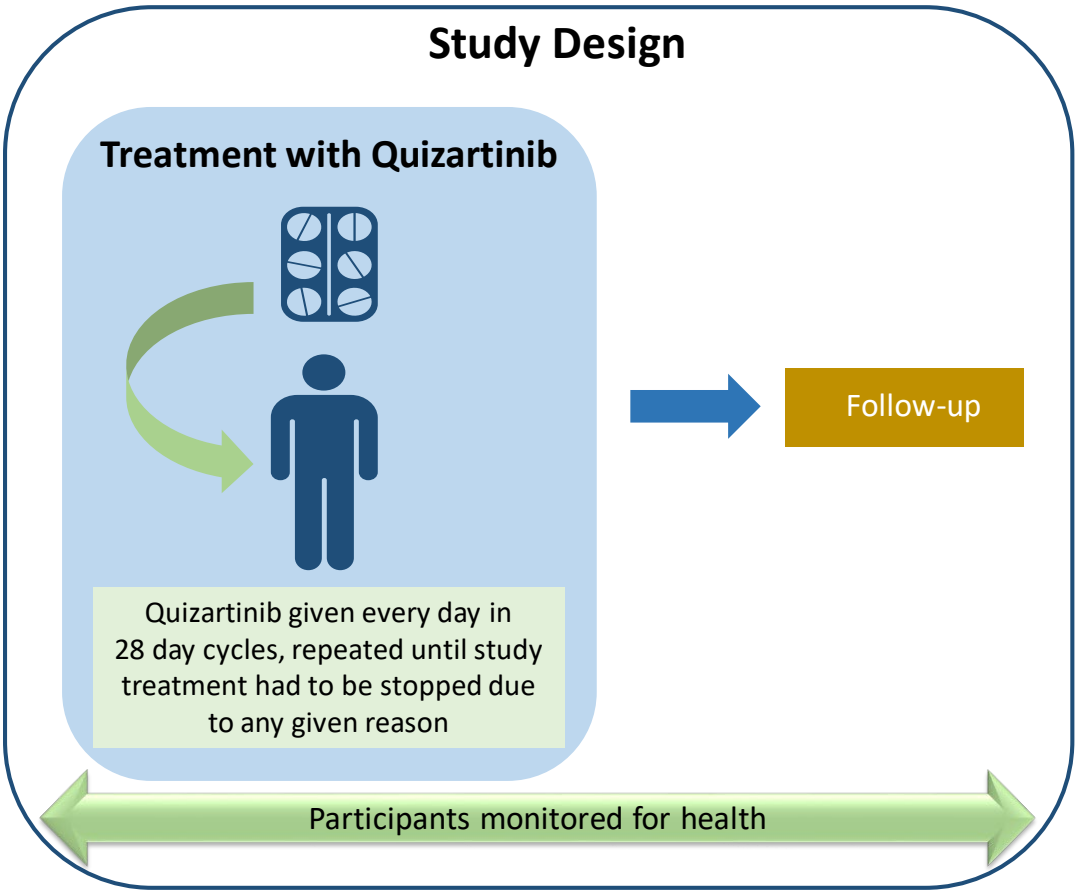
Participants took quizartinib tablets once every morning for 28 days. This cycle of treatment could be repeated until the study treatment had to be stopped due to any of the given reasons listed on the right.

Researchers collected bone marrow and blood samples from the participants throughout the study to check the effect of quizartinib on AML. They also monitored the health of the participants throughout the study.

Reasons for stopping study treatment:

- *Cancer worsening,*
- *Severe changes in electrical activity in the heart (Electrocardiogram QT prolonged),*
- *Study treatment seemed to be no longer beneficial,*
- *The amount of blood being pumped out of the heart is less than the body needs,*
- *Stem cell transplant,*
- *Participant's request to withdraw from the study treatment.*

Thirty seven participants received quizartinib and were monitored for side effects. Five of these participants tested negative for FLT3-ITD, so only 32 participants were examined to see if quizartinib was effective.



What were the key results of this study?

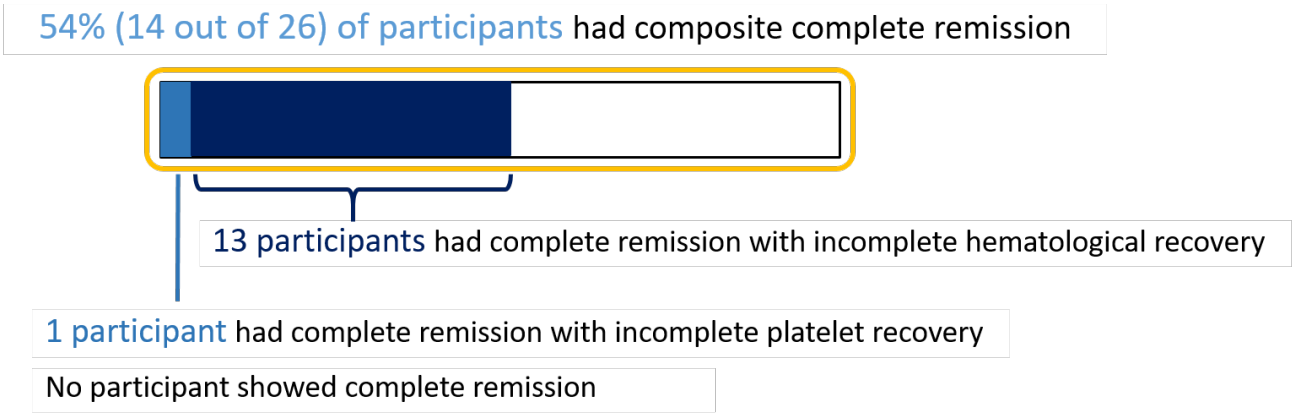
Key results from this study are shown for each initial dose group of participants collectively. This summary does not show the results from each individual participant. An individual participant's results could be different from the total group of participants. A full list of the questions the researchers wanted to answer and a detailed presentation of the results can be found on the websites listed at the end of this summary.

How many AML participants showed composite complete remission to treatment with quizartinib?

To answer this question, researchers checked how many AML participants had complete remission (CR), complete remission with incomplete platelet recovery (CRp), and complete remission with incomplete hematological recovery (CRi).

The percentage of participants who showed composite complete remission to treatment with quizartinib were:

Percentage of AML participants who showed composite complete remission to treatment with quizartinib



What were the other results of this study?

How long did AML participants live after initiating treatment with quizartinib until they died due to any cause?

Researchers measured the time from starting the treatment until the participants died due to any cause (disease or non-disease related reasons). At the end of this study, researchers found that half of the participants lived for at least 34 weeks (7.8 months) after initiating treatment with quizartinib.

How long did AML participants live until it was confirmed that the treatment did not benefit them, or their disease came back, or they died due to any cause?

Researchers measured the following events for each participant from the time they entered the study until:

- it was proven that the treatment did not benefit the participant, or
- the disease came back again after responding to the treatment, or
- the participant died due to any cause, whichever happened first.

About half of the participants who started treatment with quizartinib lived for at least 13 weeks (3 months) before any of the above events occurred.

How long did the participants receive treatment during the study?

The median duration for which the participants received quizartinib was 66 days. Median is the midpoint value. For example, the duration of the treatment for half of the participants treated with quizartinib was less than 66 days, and for the other half it was more.

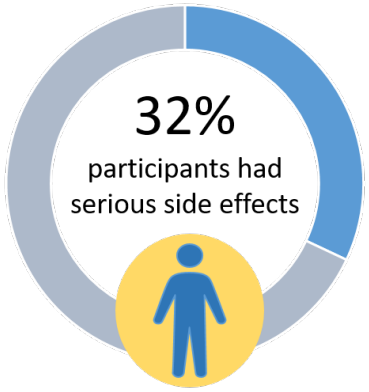
What side effects did the participants develop during the study?

Side effects are medical problems (this may range from something mild such as feeling tired or something more severe like a severe infection or other medical problem) that happened during the study, which the study doctor thought could be related to the treatments in the study.

Side effects are considered serious if they cause death, are life-threatening, cause disability, cause lasting problems, cause birth defects, or require hospitalization. Some participants stopped study treatment because of side effects.

Side effects other than those related to study treatment are not reported here. For more information on medical problems, please visit the websites listed at the end of this summary.

How many participants had serious side effects?



12 out of 37 participants reported serious side effects

Serious side effects reported by participants are shown below:

Serious Side Effects	Percentage (Number of Participants)
Abnormally low number of neutrophils accompanied by fever	**11% (4 out of 37)**
Infection caused by bacteria in the blood	**5% (2 out of 37)**
Abnormally low number of white blood cells	**3% (1 out of 37)**
Chest pain not related to heart disease	**3% (1 out of 37)**
Inflammation of lung tissue	**3% (1 out of 37)**
Large painful sores on the skin	**3% (1 out of 37)**
Low hemoglobin levels in blood	**3% (1 out of 37)**
Low number of platelets	**3% (1 out of 37)**
Lung infection	**3% (1 out of 37)**
Lung infection along with obstruction to the small airways and air sacs of the lungs (alveoli)	**3% (1 out of 37)**
Serious infection of blood due to any cause	**3% (1 out of 37)**
Skin infection caused by bacteria	**3% (1 out of 37)**

Serious Side Effects	Percentage (Number of Participants)
Swelling of the feet and hands	 **3% (1 out of 37)**
Vomiting	 **3% (1 out of 37)**

No death was reported due to side effects.

How many participants had side effects?

Side effects reported, both serious and non-serious, are presented in this section.

The most common side effects that occurred in at least 5% (5 out of 100) of participants are shown below:

Most Common Side Effects	Percentage (Number of Participants)
Low number of platelets	 **38% (14 out of 37)**
Electrical disturbance of the heart detected using ECG	 **35% (13 out of 37)**
Abnormally low number of neutrophils accompanied by fever	 **32% (12 out of 37)**
Low hemoglobin levels in blood	 **27% (10 out of 37)**
Feeling sick (the desire to vomit)	 **22% (8 out of 37)**
Low number of white blood cells	 **22% (8 out of 37)**

Most Common Side Effects	Percentage (Number of Participants)
Low number of neutrophils	 **19% (7 out of 37)**
Abnormally low number of platelets	 **11% (4 out of 37)**
Abnormally low number of white blood cells	 **8% (3 out of 37)**
Vomiting	 **8% (3 out of 37)**
Constipation	 **5% (2 out of 37)**
Decreased appetite	 **5% (2 out of 37)**
Abnormal increase in alanine aminotransferase (ALT) (one of the tests of how the liver is functioning)	 **5% (2 out of 37)**
Altered taste	 **5% (2 out of 37)**
Diarrhea	 **5% (2 out of 37)**
Infection caused by bacteria in the blood	 **5% (2 out of 37)**
Sore and inflamed mouth	 **5% (2 out of 37)**
Liver disorder	 **5% (2 out of 37)**

Most Common Side Effects	Percentage (Number of Participants)
Liver function test increased	5% (2 out of 37)
Lung infection	5% (2 out of 37)
Raised red bump on the skin	5% (2 out of 37)
Swelling of the feet and hands	5% (2 out of 37)
Weakness, numbness, and pain from nerve damage in the hands and feet	5% (2 out of 37)

How many participants had to stop treatment because of side effects?

One participant stopped the treatment due to an increase in a blood protein called lipase that helps the body to digest fats.

How was this study useful for patients and researchers?

This study helped researchers learn about how effective quizartinib was at treating Japanese patients with refractory or relapsed FLT3-ITD positive AML.

Findings from this study were used to support the approval of quizartinib for treating Japanese patients with AML who have tested positive for FLT3-ITD mutation. Other studies on quizartinib are ongoing.

Please remember, this summary only shows the results of a single study. Other studies may have different findings. Please talk to a doctor before changing any treatment you are taking or if you have any questions about these study results.

Where can I learn more about this study?

You can find more information about this study on the following website:

- www.clinicaltrials.gov: Use the NCT identifier NCT02984995 in the search field.

Please remember that the results on this website may be presented in a different way. If you were a study participant and have questions about the results of this study, please speak with the doctor or staff at your study site.

Full study title: A Phase 2 Open-label, Single-arm Study of Quizartinib (AC220) Monotherapy in Japanese Patients with FLT3-ITD Positive Refractory or Relapsed Acute Myeloid Leukemia

Sponsor: Daiichi Sankyo, Inc.

Sponsor contact information:

211 Mount Airy Road, Basking Ridge, NJ 07920

Email: CTRInfo@dsi.com

Phone number: 1-908-992-6640

for any queries related to the summary.

Date of this summary: 04 January 2021

This summary was prepared by Kinapse Ltd, a Syneos Health® company.