



Clinical Results Summary

A clinical study to learn about the safety and effects of quizartinib in people with a type of blood cancer called acute myeloid leukemia who have had a stem cell transplant

Protocol number: 2689-CL-0011

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 for people affected with a type of blood cancer called acute myeloid leukemia who have had a stem cell transplant. 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) after stem cell transplant

Researchers were looking for a better way to treat people with a type of blood cancer called acute myeloid leukemia, or AML. The participants in this study were diagnosed with FLT3-ITD positive AML and had recently received a stem cell transplant when the signs and symptoms of their cancer had disappeared (remission).

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 safe and effective quizartinib is at treating patients with FLT3-ITD positive AML when given as maintenance therapy after a stem cell transplant. Maintenance therapy is a treatment that is given to help keep cancer from coming back after it has disappeared following the initial therapy.

Treatment given in this study



(or)



Quizartinib

An investigational treatment being tested for the treatment of AML participants who were tested positive for FLT3-ITD and have had a stem cell transplant

Main purposes of this study

The main questions the researchers wanted to answer in this study were:



What were the Dose-Limiting Toxicities (DLTs) caused by quizartinib?

Defined as certain severe medical toxicities caused by quizartinib.



What was the Maximum Tolerated Dose (MTD) of quizartinib?

Defined as highest dose of treatment that does not cause too many DLTs in participants.



How many participants had side effects during the study?

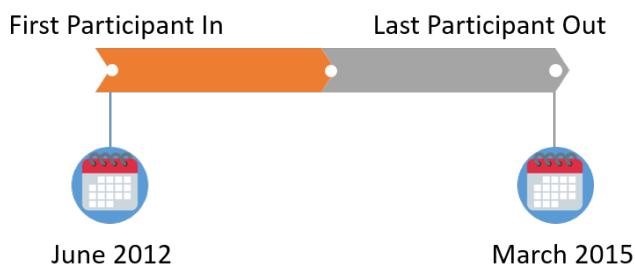
Other purpose of this study

Researchers also wanted to answer the following question:

- How long did AML participants live after initiating treatment with quizartinib until they died due to any cause? This is also called 'Overall Survival'.

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

How long was this study?



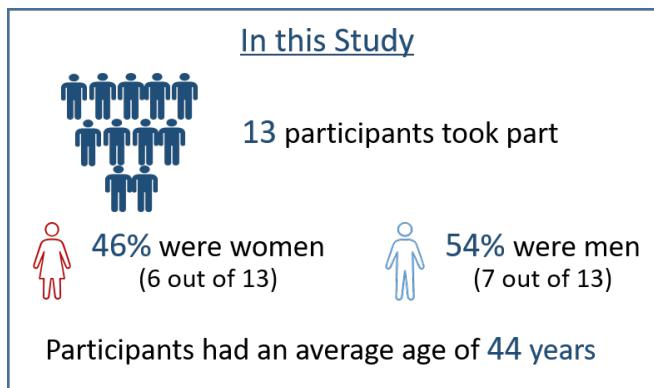
This study was designed in such a way that the participants could continue to take quizartinib for up to 24 treatment cycles as long as they did not meet certain criteria for discontinuing treatment.

The first participant entered the study on 14 June 2012.

The sponsor ended this study early for administrative and resource issues which were not related to any safety or effects of quizartinib, after 13 participants were enrolled. The study ended on 17 March 2015. This summary is based on that report.

Who was in this study?

This study included 13 participants from the United States.





Participants could take part in this study if they:

- were diagnosed with AML and had received a stem cell transplant within 1 to 2 months of taking their first dose of quizartinib
- were at least 18 years of age
- were free from AML disease
- had normal neutrophil and platelet counts (neutrophil is a type of white blood cell that fights bacteria and platelet is a type of blood cell that helps in preventing/stopping bleeding)
 - had no complaints and no evidence of disease, OR had minor signs or symptoms of disease but were able to
 - carry on normal activity, OR had some disease symptoms but were able to carry on normal activity with effort, OR could manage self-care but were unable to carry on normal activity or do active work, OR could manage self-care but required occasional assistance



Participants could not take part in this study if they:

- had any other diseases or abnormal laboratory tests that could prevent them from attending study visits and assessments
- received standard therapy or any other therapy for AML within 3 weeks of taking their first dose of quizartinib
- were previously treated with quizartinib and their AML came back during the treatment
- had any major heart problems such as a heart attack within a year before participating in the study

What happened during this study?

This was a Phase 1 study. Phase 1 studies are done to find out how new study treatment works in a small number of patients. This helps researchers understand what happens to the study treatment in the body, and if there are any side effects.

This study was “open label”. This means that both the researchers and the participants knew which treatment was given to which participant.

Participants who had a stem cell transplant for their AML were screened to find out if they could take part in this study. Participants who passed screening took their first dose of quizartinib 1 to 2 months after their stem cell transplant.

Participants took 1 or 2 quizartinib tablets by mouth or powdered form of quizartinib by mouth once every morning at least 1 hour before or 2 hours after a meal, for 28 days (1 cycle). This cycle of treatment could be repeated for up to 24 treatment cycles until the study treatment had to be stopped due to any of the given reasons listed above.

The study was divided into 2 parts.

Part 1

Part 1 was done to find the highest dose of quizartinib that participants could tolerate.

The 13 participants who passed screening were assigned to 2 groups: 7 participants in the quizartinib 40 milligram (mg) group and 6 participants in the quizartinib 60 mg group. Researchers started by giving 40 mg of quizartinib to the first group of participants. If this dose was considered to be safe by the researchers, the next group of participants received 60 mg of quizartinib.

Part 2

Part 2 of this study was planned to find out more about the safety and effects of the dose of quizartinib selected during Part 1. However, the study was terminated before Part 2 could begin. Based on another clinical study that compared 30 mg versus 60 mg daily quizartinib, researchers decided that 60 mg was the maximum dose to be taken forward into further studies.

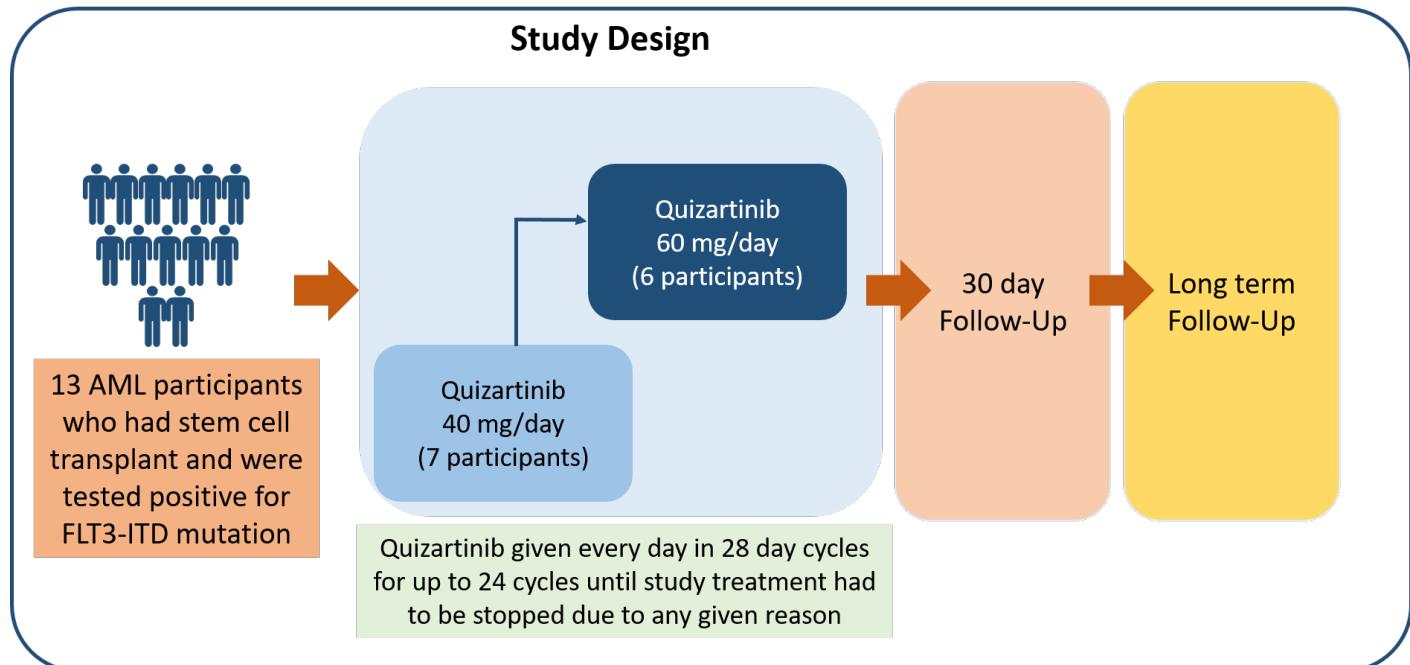
Participants visited the researchers between 30 days and 35 days after the last dose of study treatment. During these visits, researchers collected information on the health of each participant. During the long term follow-up, participants’ well-being was checked via a phone call every 3 months.



Reasons for stopping study treatment

- *Participant’s cancer came back*
- *Changes in electrical activity in the heart (Electrocardiogram QT prolonged) that did not resolve within 2 weeks*
- *Low number of neutrophils or platelets*
- *Developed Dose-Limiting Toxicities*

Researchers also monitored the health of the participants throughout the study.

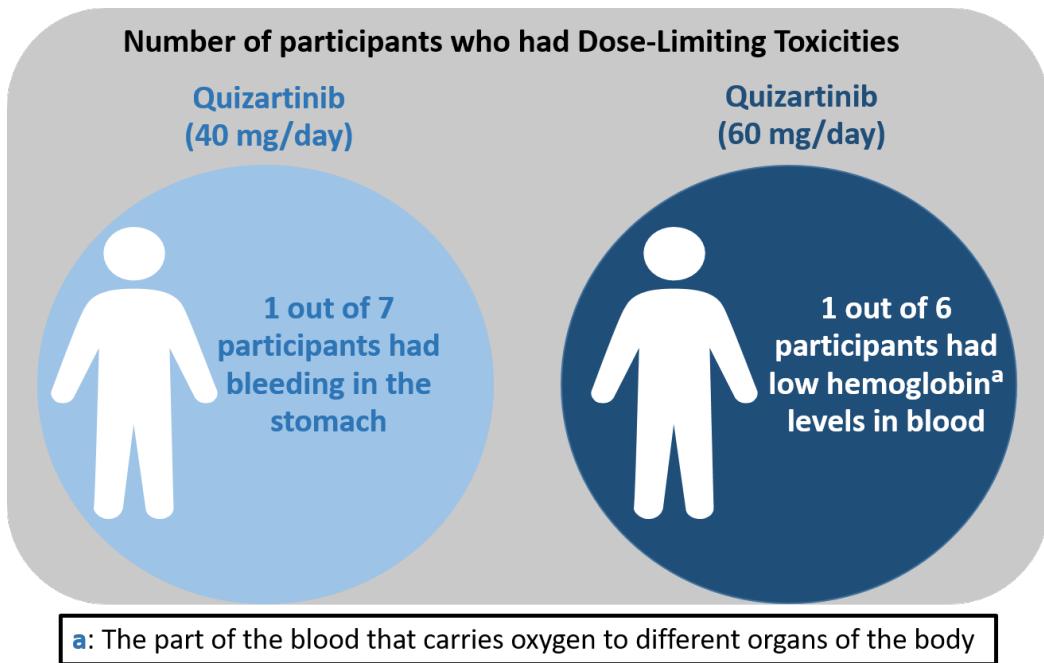


What were the key results of this study?

Key results from this study are shown for the total group of participants as average results. 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.

What were the Dose-Limiting Toxicities (DLTs) caused by quizartinib?

The number of DLTs helped researchers decide whether the 40 mg dose was safe and if the next group of participants could receive the 60 mg dose.



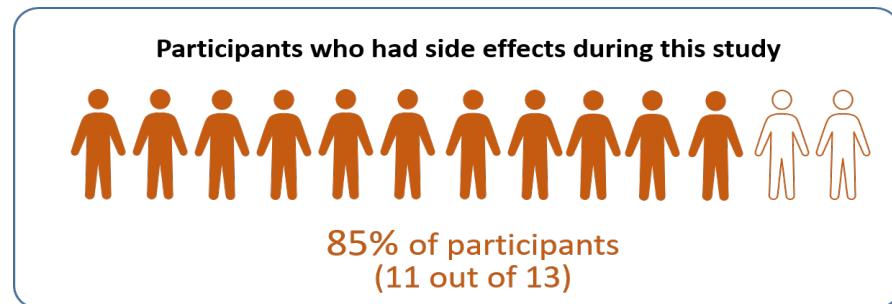
What was the Maximum Tolerated Dose (MTD) of quizartinib?

The MTD is the highest dose of treatment that does not cause too many DLTs in participants.

This study indicated that both 40 mg and 60 mg were well tolerated by participants with AML after a stem cell transplant. The highest dose of quizartinib that participants could tolerate after a stem cell transplant was not identified in this study. Doses above 60 mg daily were not explored in this study.

How many participants had side effects during the study?

This section provides the overall number of participants who had side effects related to the study treatment during the study. Details on what medical problems participants had during the study are presented below.



What were the other results of this study?

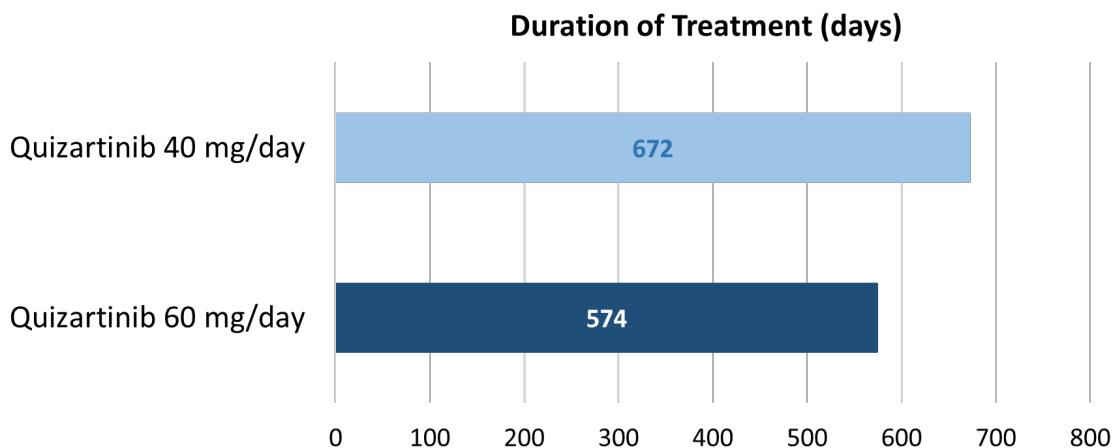
How long did AML participants live after initiating treatment with quizartinib until they died due to any cause?

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 the study, researchers found that 10 out of 13 participants were alive. Participants lived between **13 weeks (3 months)** and **142 weeks (2 years 9 months)** after starting treatment with quizartinib.

How long did the participants receive treatment during the study?

The figure below shows the median duration for which the participants took either **40 mg/day** or **60 mg/day** quizartinib. Median means the midpoint value for a group.

Participants who were in quizartinib 40 mg/day group received the drug for **672 days** (or about 1 year **10 months**), while those who were in quizartinib 60 mg/day group received the drug for **574 days** (or about 1 year **7 months**).



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 researchers 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.

Study participants who had serious side effects

In this study, side effects were monitored for 13 participants: 7 participants in quizartinib 40 mg/day group and 6 participants in quizartinib 60 mg/day group.

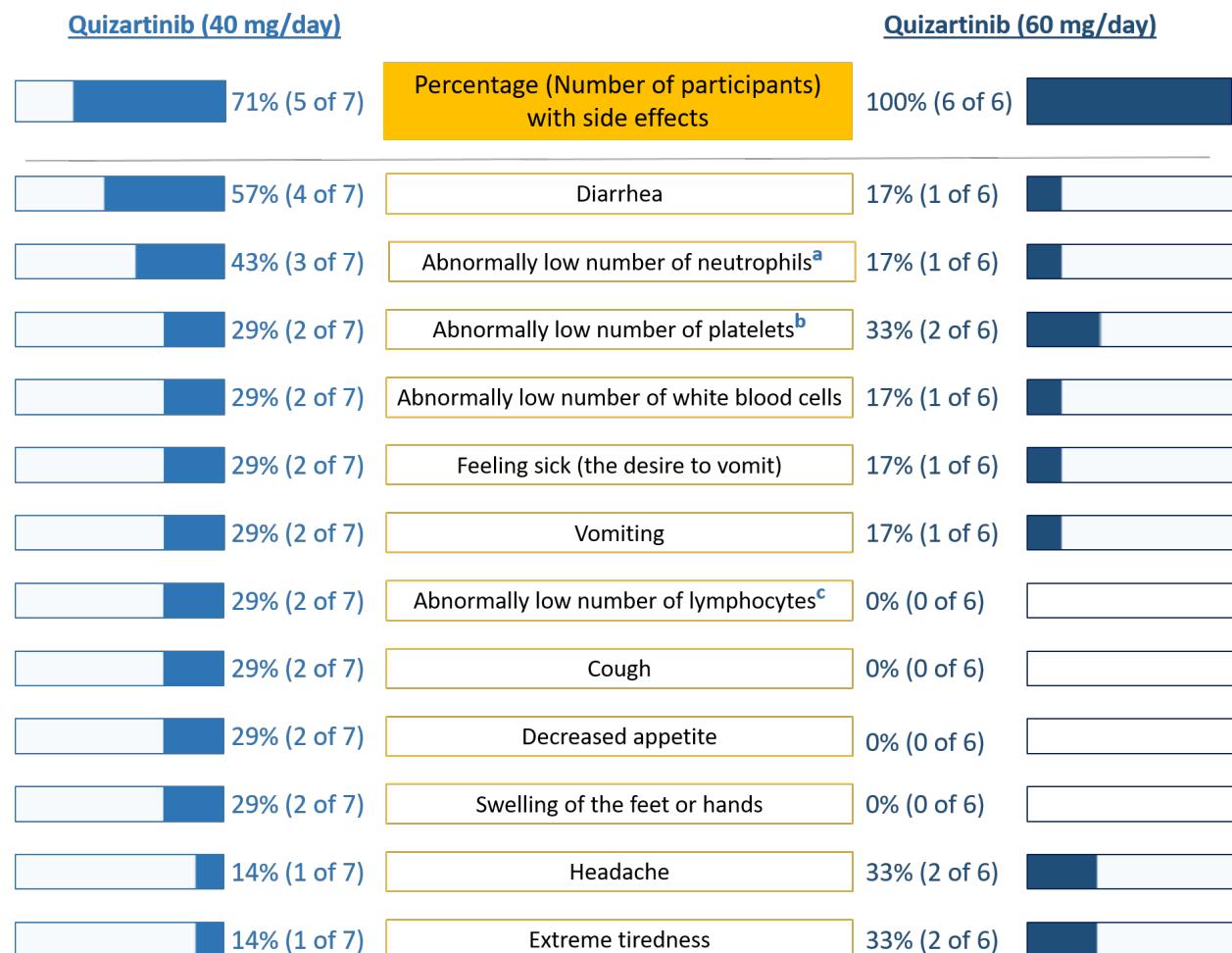
40 mg group: 3 out of 7 (43%) participants had serious side effects. The serious side effects reported were abnormally low number of neutrophils (a type of white blood cell that fights bacteria), bleeding in the stomach, eye stroke (blockage of blood flow to the eye), and low hemoglobin levels in blood (part of the blood that carries oxygen to different organs of the body).

60 mg group: 3 out of 6 (50%) participants had serious side effects. The serious side effects reported were headache, loss of or injury to the outermost layer of the cornea (the transparent layer forming the front of the eye), and lung infection.

There were no deaths due to the study treatment.

How many participants had most common side effects?

The most common side effects, both serious and non-serious, reported by at least 2 participants in any group are reported below:



a: A type of white blood cell that fights bacteria

b: A type of blood cell that helps in preventing/stopping bleeding

c: A type of white blood cell that fights virus infection

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

Two participants stopped treatment early due to side effects. One participant in the 40 mg group stopped the treatment early due to abnormally low number of neutrophils (a type of white blood cell that fights bacteria). One participant in the 60 mg group stopped the treatment early due to loss or injury to the outermost layer of the cornea (the transparent layer forming the front of the eye).

How was this study useful for patients and researchers?

This study helped researchers learn about a safe dose of quizartinib that can help to keep the AML from coming back in patients after a stem cell transplant.

Findings from this study may be used in other studies to learn whether patients with AML are helped by this treatment. 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 NCT01468467 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.

Full study title: A Phase 1 Study of AC220 (ASP2689) as Maintenance Therapy in Subjects with Acute Myeloid Leukemia Who Have Been Treated With an Allogeneic Hematopoietic Stem Cell Transplant

Sponsor: Daiichi Sankyo, Inc.

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Date of this summary: 14 January 2021

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