Daiichi-Sankyo

Clinical Results Summary

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

Protocol number: CP0001

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 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 acute myeloid leukemia, or AML. The participants in this study:

- did not respond to their first cycle of treatment (known as refractory AML); or
- did respond and were free of disease but then their AML came back after receiving at least the first cycle of treatment (known as relapsed AML); or
- were not suitable to receive initial (first) chemotherapy treatment due to their age, health status or other reasons, according to the researcher's judgment.

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.

At this time, the main treatment option 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.

In this study, researchers wanted to learn more about the safety and effects of quizartinib in AML patients.

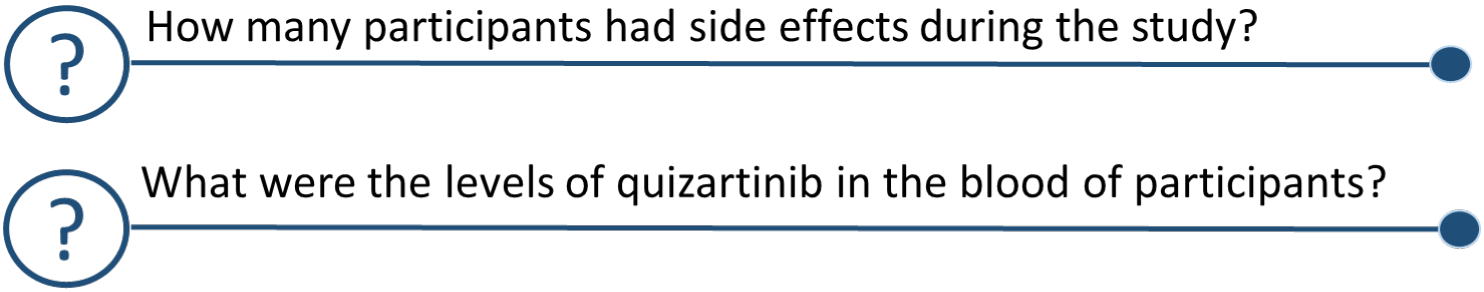
Treatment given in this study

Quizartinib

An investigational drug being tested for the treatment of AML participants

Main purpose of this study

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



Other purpose of this study

Researchers also wanted to answer the following questions:

- What was the best response the AML participants had to treatment with quizartinib?

Best response could be either Composite complete remission (CRc) or Partial remission (PR).

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 participant's 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 participant's 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 participant's bone marrow were cancer cells, with incomplete recovery of platelets; plus
- **Complete remission with incomplete hematological recovery**, which is also called "**CRi":** CRi meant less than 5% of cells in the participant's bone marrow were cancer cells, with incomplete recovery of neutrophils, with or without complete recovery of platelets. The participant may or may not have needed blood or platelet transfusion.

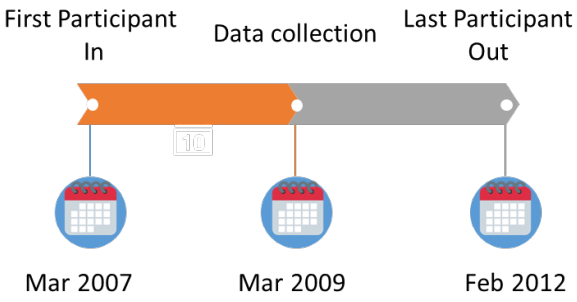
*Neutrophils are a type of white blood cells that fight bacteria. Platelets are a type of blood cells that help in preventing/stopping bleeding.

Partial remission was defined as disappearance of at least 50% of their blood cancer cells after treatment.

- How long did participants live with their cancer before it got worse or the patient died due to any cause of death? This is also called '**Progression Free Survival**'.

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

How long was this study?



The study was designed in such a way that the participants could continue in it as long as they benefited from the treatment and their AML did not get worse, and they didn't have any serious side effects. A serious side effect could have caused a participant to discontinue their treatment with quizartinib. The first participant was enrolled in the study in March 2007.

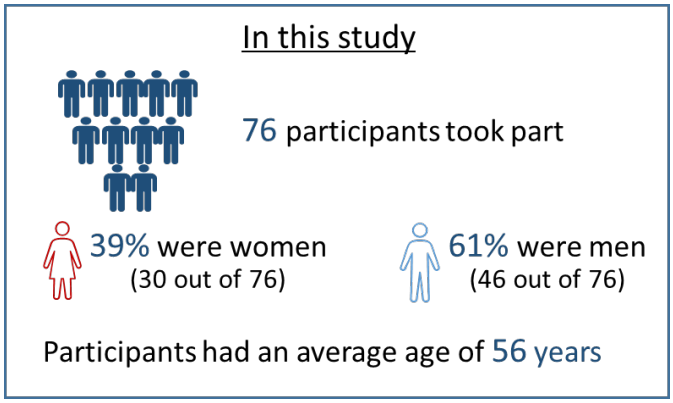
The results were collected up to February 2012 and a study report was created. This summary is based on that report.

Who was in this study?

This study included a total of 76 participants from 2 countries: 57 from the United States and 19 from Georgia.

Participants could take part in this study if they:

- were diagnosed with AML,
- were at least 18 years old,
- did not respond to their first treatment, or did respond and were free of disease but then their AML came back after receiving their first treatment, or
- were never treated as they were not able to be treated with induction chemotherapy because of their age, health status or other reasons,
- 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 self-care and be out of bed for more than 50 % of waking hours, OR able to manage limited self-care and be out of bed for less than 50 % of waking hours,
- did not have another type of blood cancer, specifically acute promyelocytic leukemia,



- did not have severe side effects from prior chemotherapy or surgery,
- did not have surgery or radiation therapy within 4 weeks before participating in the study,
- did not have any major heart problems such as heart failure within 3 months before participating in the study,
- did not have hepatitis B or C, or Human Immunodeficiency Virus (HIV), and
- did not have bone marrow transplant within 2 months before the study.

What happened during this study?

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

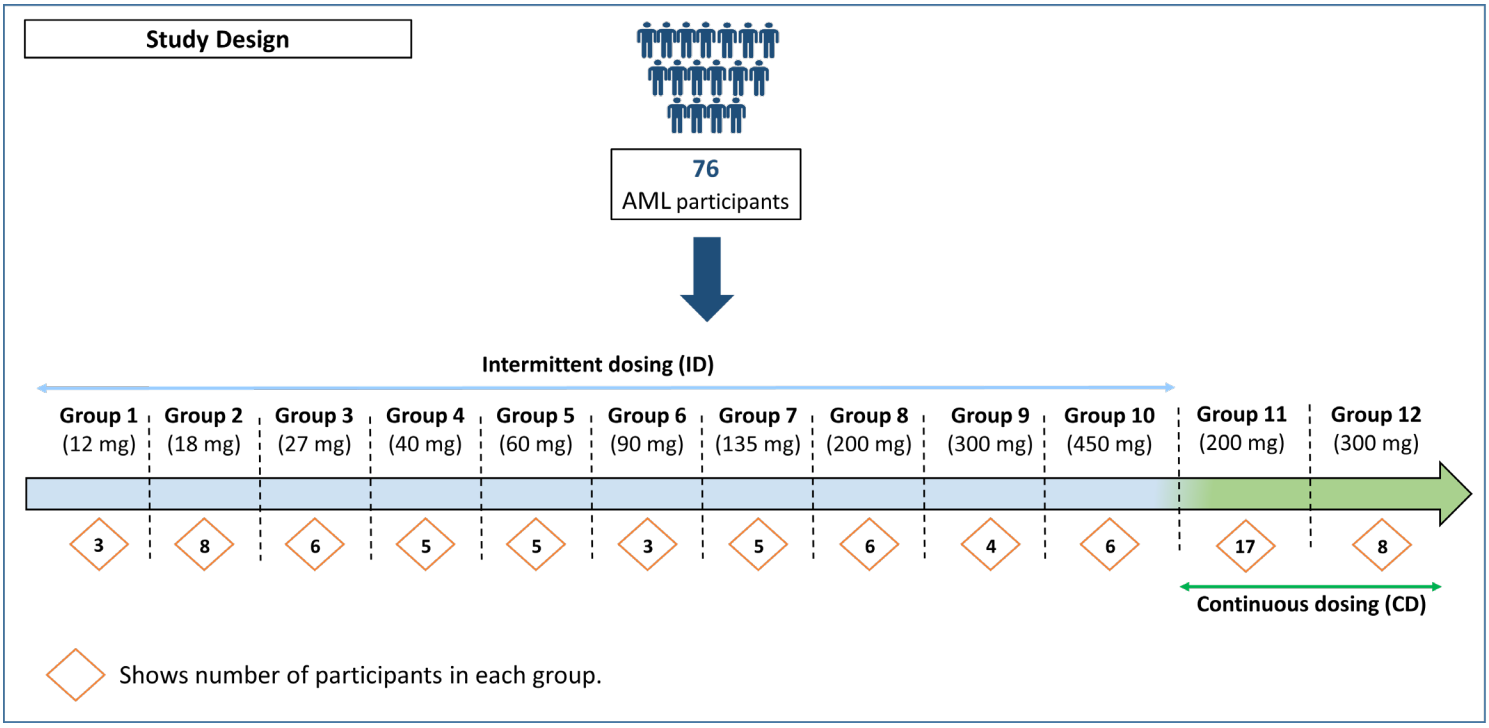
This was an "open label" study. This means that the study doctors, the participants and the researchers knew what treatment was given. All participants took quizartinib as an oral solution. They continued to receive quizartinib as long as they benefited from the treatment without any serious side effects.

Researchers started by giving participants 12milligrams (mg) of quizartinib. Once the researchers considered this dose of quizartinib safe, the next group of participants received a higher dose of quizartinib. This process was repeated with increasingly higher doses, until researchers identified the highest dose of quizartinib that could safely be given to participants.

When the study started, participants took quizartinib daily for 14 continuous days, followed by 14 days of rest (1 cycle of 28 days). This dosing regimen was called intermittent dosing (ID). The ID doses levels studied ranged from 12 mg to 450 mg per dosing day.

While the study was ongoing, the dosing regimen was changed. New participants entering the study at that point took quizartinib daily for 28 days (1 cycle) with no breaks between cycles. This dosing regimen was called continuous dosing (CD). The CD doses levels studied were 200 and 300 mg/day. The researchers identified **200 mg/day CD** as the highest dose of quizartinib that could safely be given to participants.

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.



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 website listed at the end of this summary.

How many participants had side effects during the study?

Side effects are medical problems (this may range from something mild such as a feeling tired or something more severe like a severe infection or other medical problem) that happened during the study, which the study doctor (investigator) thought could be related to the treatments in the study. Detailed information about side effects reported by participants is presented in the section 'What side effects did the participants developed during the study?'

During the study, 39 (51%) out of 76 participants had side effects.

What were the levels of quizartinib in the blood of participants?

To answer this question, researchers took blood samples from participants in each group on Day 1 and Day 8 of treatment with quizartinib. They measured the highest level of quizartinib in the participants' blood on Day 1 and Day 8 of treatment. However, the results of this measurement were unreliable.

What were the other results of this study?

What was the best response the AML participants had to treatment with quizartinib?

Best response could be either Composite complete remission or Partial remission.

To answer this question, researchers checked how many AML participants had composite complete remission or partial remission. The definitions of these terms can be found on Pages 2 and 3 of this document.

Overall, 30% (23 out of 76) of participants showed **composite complete remission or partial remission** after treatment with quizartinib during the study.

13% (10 out of 76) of participants had **composite complete remission** to treatment with quizartinib.

- 3% (2 out of 76) of participants had **complete remission**.
- 4% (3 out of 76) of participants had **complete remission with incomplete platelet recovery**.
- 7% (5 out of 76) of participants had **complete remission with incomplete hematological recovery**.

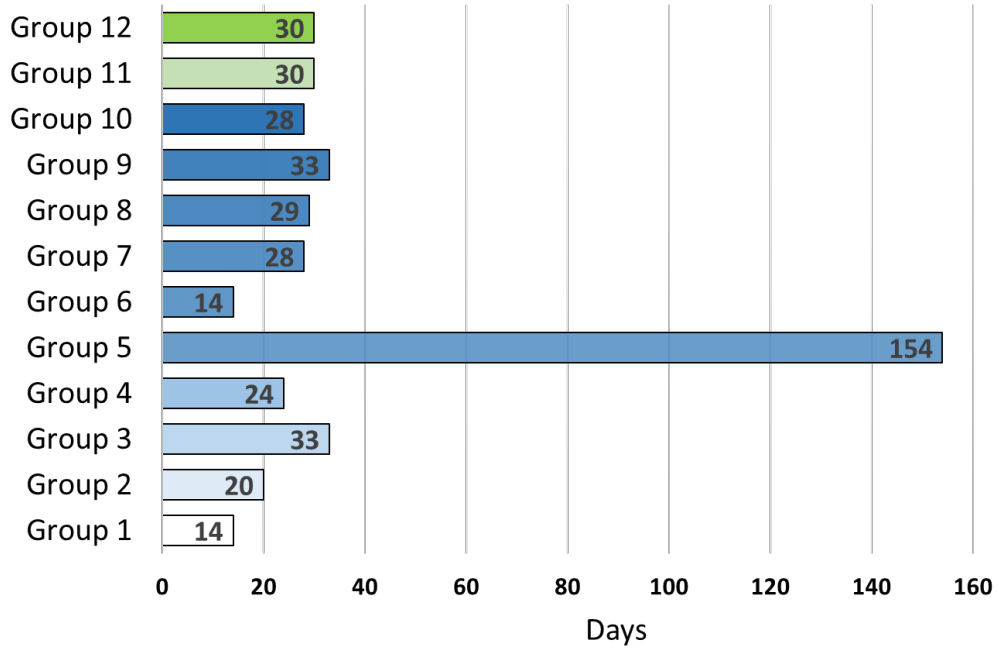
17% (13 out of 76) of participants had **partial remission** after treatment with quizartinib.

How long did participants live with their cancer before it got worse or led to death?

For half of the participants, it took at least 9 weeks (2 months) for their cancer to start getting worse or to lead to death.

How long did the participants receive treatment during the trial?

The median duration for which the participants received different doses of quizartinib during the trial is presented below. Median means the midpoint value for a group. For example, in the group of participants who were treated with 12 mg quizartinib, the duration of the treatment for half of them was less than 14 days and for the other half it was more.



What side effects did the participants developed 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?

During the study 6 (8 %) out of 76 participants had serious side effects. Serious side effects reported by participants were:

Serious Side Effects	Percentage (Number of Participants)
Changes in corrected electrical activity in the heart[a] (Electrocardiogram QT corrected interval prolonged)	3% (2 out of 76)
Changes in electrical activity in the heart[a] (Electrocardiogram QT prolonged)	1% (1 out of 76)
Infection in the lungs	1% (1 out of 76)
Low number of platelets[b]	1% (1 out of 76)
Vomiting	1% (1 out of 76)

a: Detected using an Electrocardiogram (ECG) of the heart
b: Platelets are a type of blood cell that helps to stop bleeding

No death was reported due to side effects.

How many participants had side effects?

The most common side effects, both serious and non-serious, that occurred in at least 10% (10 out of 100) of participants were:

Side Effects	Percentage (Number of Participants)
Feeling sick to your stomach	16% (12 out of 76)
Changes in electrical activity in the heart[a] (Electrocardiogram QT prolonged)	12% (9 out of 76)
Change in sense of taste	11% (8 out of 76)
Vomiting	11% (8 out of 76)

a: Detected using an Electrocardiogram (ECG) of the heart

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

Percentage of participants who stopped quizartinib due to side effects

(4 out of 76 had stopped quizartinib)

The most common side effects that caused participants to stop quizartinib treatment were changes in electrical activity in the heart (Electrocardiogram QT prolonged) and bleeding in the stomach.

How was this study useful for patients and researchers?

This study helped researchers to learn about the safety and effects of quizartinib in people with AML tested negative or positive for FLT3-ITD alteration (or mutation). Based on the results of this study, researchers identified **200 mg/day CD** as the maximum dose of quizartinib that could safely be given to patients in further studies.

Findings from this study may be used in other studies to learn whether patients with AML are helped by this treatment. Other studies for 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 NCT00462761 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 1 Open-Label, Sequential Dose Escalation Study Investigating the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AC220 when Administered Daily to Patients with Relapsed or Refractory 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

Date of this summary: 02 February 2021

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