Daiichi-Sankyo

Clinical Results Summary

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

Protocol number: AC220-A-J101

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 following at least one cycle of previous treatment (known as refractory AML) or
- responded but their disease came back again after receiving prior treatment (known as relapsed AML).

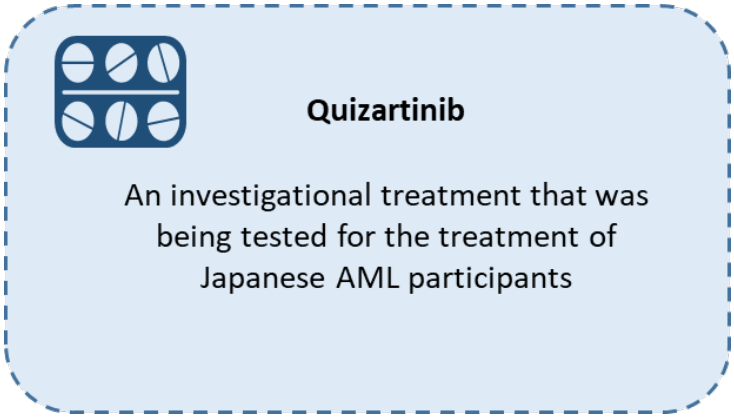
AML is a cancer of the blood and the bone marrow. The bone marrow is found in the center of most bones, where new healthy blood cells are made. AML starts in the bone marrow and prevents it from making normal blood cells. The abnormal (cancer) cells build up in the bone marrow, so there are fewer healthy 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 relapsed or refractory AML patients in Japan 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. However, chemotherapy has not been very beneficial in treating Japanese AML patients, and no standard treatment is available yet.

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. FLT3-ITD positive AML is often severe, does not respond well to standard treatment and is likely to come back even after treatment. Quizartinib is designed to work against AML cells with this genetic mutation.

Researchers wanted to find out about the safety of different doses of quizartinib and how the body affected blood levels (pharmacokinetics) of quizartinib in people with relapsed or refractory AML. Participants in this study had relapsed or refractory AML, whatever their FLT3-ITD status (it could be positive or negative).

Treatment given in this study

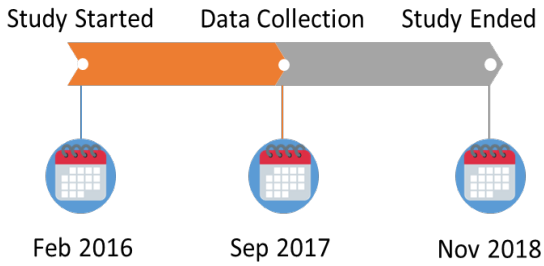


Main purposes of this study

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

- What side effects did the participants develop during the study?
- What were the levels of quizartinib in the blood of participants?

How long was this study?



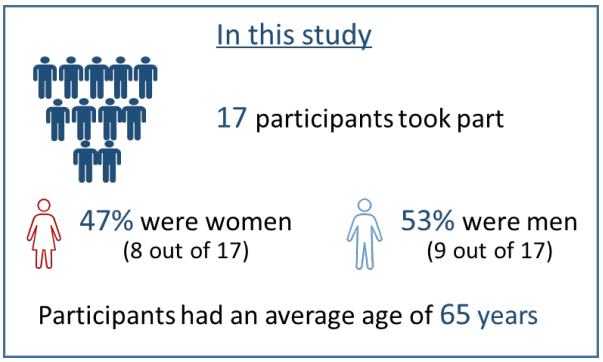
The study was designed in such a way that the participants could continue in it as long as they did not meet certain criteria for stopping study treatment.

The first participant entered the study in February 2016. The results were collected up to September 2017 for the study report. This summary is based on that report. The study completed as planned in November 2018.

Who was in this study?

This study included 17 participants from 8 study sites in Japan.

Participants could take part in this study if they:



- were diagnosed with AML or had myelodysplastic syndrome (MDS – another type of blood cancer in which blood forming cells become abnormal) that progressed to AML,
- were Japanese and were 20 years and above,
- have not received any previous treatment with quizartinib,
- did not respond to their first AML treatment, or did respond and were free of disease but their AML came back,
- did not have treatment options that gave long-lasting effects, could not complete a treatment to cure their AML OR did not have any other effective treatment options,
- 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 major heart problems such as an irregular heart rhythm,
- 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 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 study was “open label”. This means that the participants and the researchers knew what treatment was given.

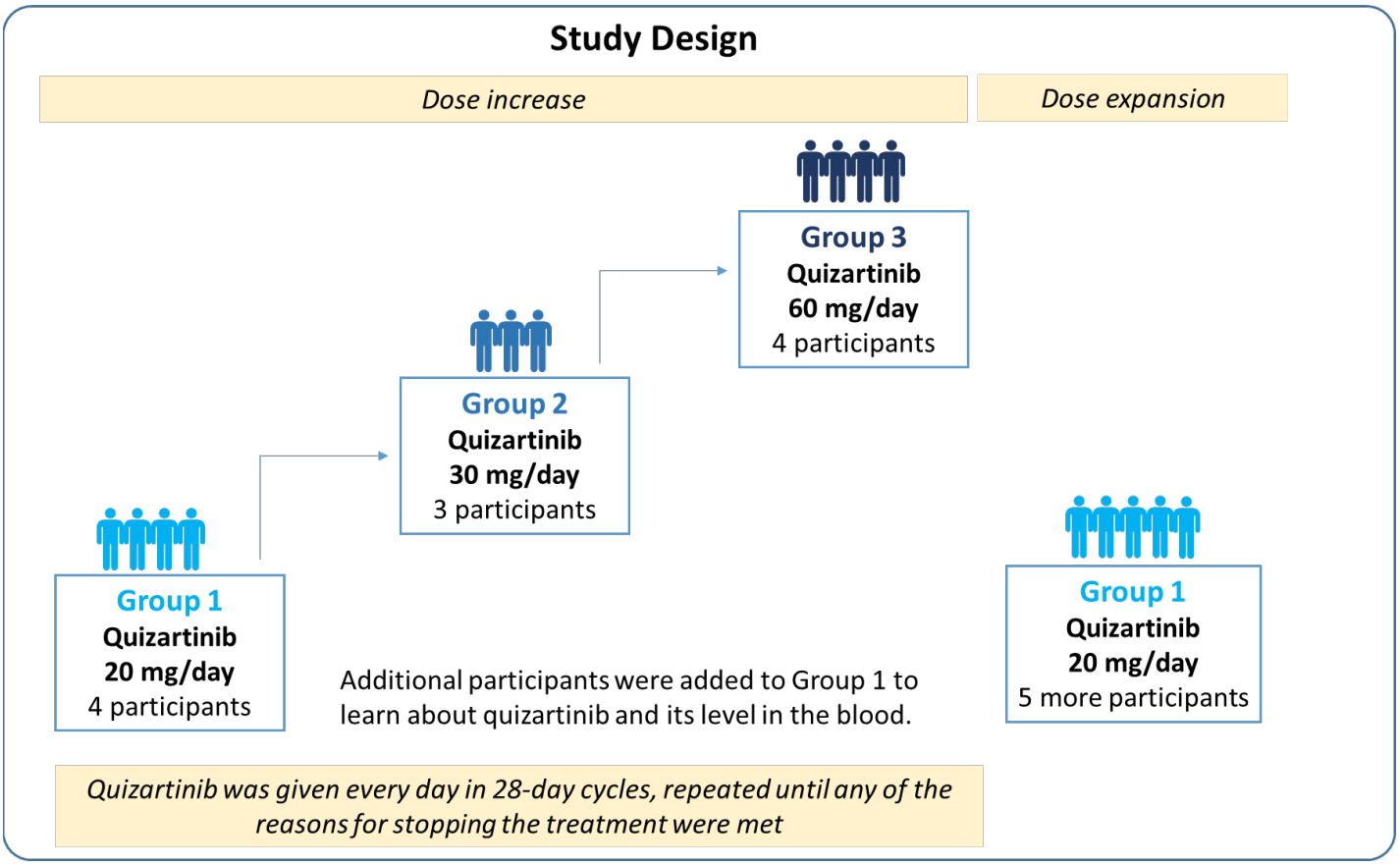
Participants were screened to find out if they could take part in the study.

Reasons for stopping study treatment

- *Cancer worsening*
- *Life threatening side effects caused by quizartinib or severe changes in electrical activity in the heart (Electrocardiogram QT prolonged).*
- *Need to reduce the dose a second time*
- *Poorly following treatment schedule or medical advice*
- *Participant’s request to withdraw from the study treatment*

Participants took quizartinib tablets once every morning for 28 days (1 cycle). This cycle of treatment could be repeated until the study treatment had to be stopped due to any of the given reasons listed above.

Researchers started by giving 20 milligrams (mg) of quizartinib to the first group of participants. Once the researchers considered this dose of quizartinib safe, the next group of participants received 30 mg of quizartinib. Once the researchers considered this dose of quizartinib safe, the next group of participants received 60 mg of quizartinib. The highest dose of quizartinib that participants could tolerate was not identified. This study indicated that 20 mg, 30 mg and 60 mg doses were well tolerated by participants and doses higher than 60 mg daily were not explored.



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 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 quizartinib are not reported here.

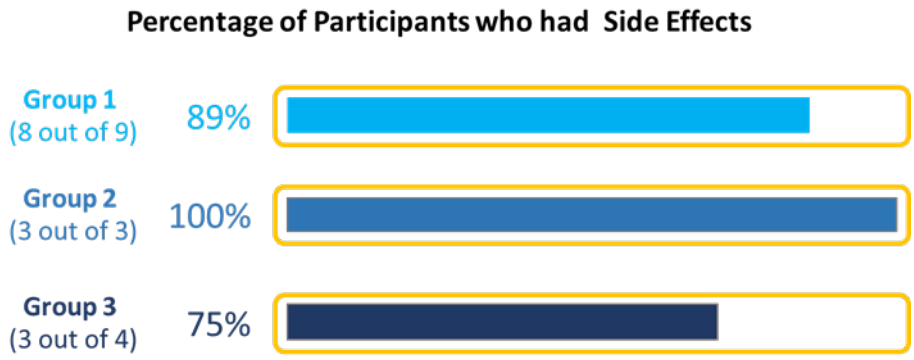
How many participants had serious side effects?

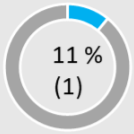
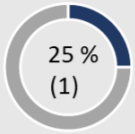
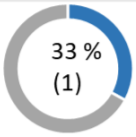
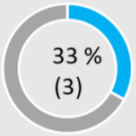
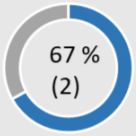
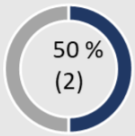
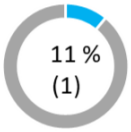
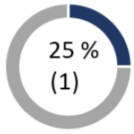
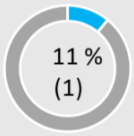
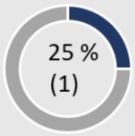
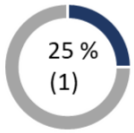
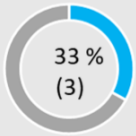
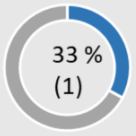
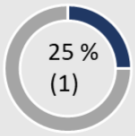
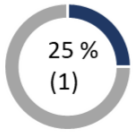
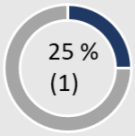
Two out of 16 participants had serious side effects. One participant in the 20 mg group had a fungus infection. It is named after the fungus that caused it (*Aspergillus)*. Another participant in the 60 mg group had a lung infection.

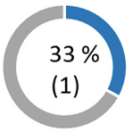
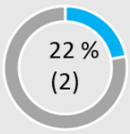
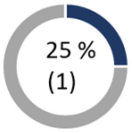
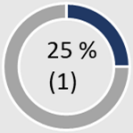
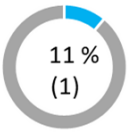
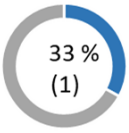
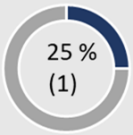
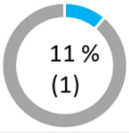
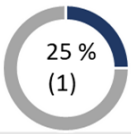
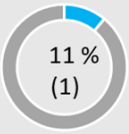
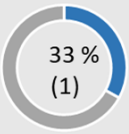
There were no deaths related to quizartinib reported during this study.

How many participants had side effects?

The side effects, both serious and non-serious, reported by at least 20% (1 out of 5) of participants in any group are reported below:



Side Effects	Group 1 (9 participants) 20 mg/day	Group 2 (3 participants) 30 mg/day	Group 3 (4 participants) 60 mg/day
Abnormally low number of neutrophils[a] accompanied by fever		0	
Altered taste	0		0
Changes in electrical activity in the heart[b] (Electrocardiogram QT prolonged)			
Decreased appetite		0	
Diarrhea		0	
Dizziness	0	0	
Feeling sick (the desire to vomit)			
Fever	0	0	
Fluid filled sacs on skin. It could be caused by several reasons eg. infection or inflammation of the skin	0	0	

Side Effects	Group 1 (9 participants) 20 mg/day	Group 2 (3 participants) 30 mg/day	Group 3 (4 participants) 60 mg/day
Inflammation of the colon	0		0
Low number of white blood cells		0	0
Lung infection	0	0	
Pneumonia	0	0	
Shingles, which is a painful rash occurring in a stripe caused by chicken pox virus			0
Skin disease with fever and high number of white blood cells	0	0	
Sore and inflamed mouth		0	
Vomiting			0

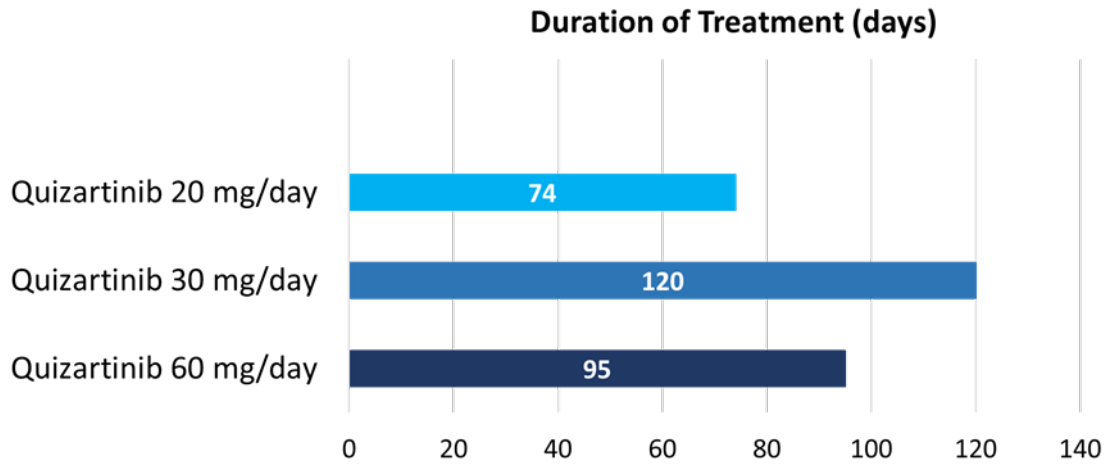
a: A type of white blood cell that fights bacteria
b: Detected using ECG of the heart

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

One participant discontinued the treatment due to a fungus infection (caused by *Aspergillus*).

How long did the participants receive treatment during the study?

The participants who took quizartinib 30 mg/day were in the study longer than the participants in other two groups. The figure below shows the median duration for which the participants received different doses of quizartinib. Median means the midpoint value for a group. For example, in the group of the participants who were treated with quizartinib 20 mg/day, the duration of the treatment for half of them was less than 74 days and for the other half it was more.



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

To answer this question, the researchers took blood samples from participants in each group on Day 15 of their treatment with quizartinib. Blood samples were also taken from participants on other days. The body breaks down quizartinib into another substance called AC886. AC886 has similar effects in the body to quizartinib. So the researchers also measured the levels of AC886 in participants' blood during the study. The researchers measured the following:

- The total level of quizartinib and AC886 in participants' blood on Day 15 of treatment.
- The highest level of quizartinib and AC886 in participants' blood on Day 15 of treatment.

The average results of these measurements are presented below. Total levels of quizartinib and AC886 in the participants' blood are measured in ng·h/mL*. The highest level of quizartinib and AC886 in blood was measured in ng/mL.

Researchers found that the levels of quizartinib and AC886 in the participants' blood were similar to those seen in other studies. They also discovered that total levels and highest levels of quizartinib and AC886 increased as the dose of quizartinib increased.

Quizartinib AC886	Group 1 (9 participants) 20 mg/day	Group 2 (3 participants) 30 mg/day	Group 3 (4 participants) 60 mg/day
The **total level** of **quizartinib** in blood (ng·hr/mL)	**1280**	**2010**	**5080**
The **total level** of **AC886** in blood (ng·h/mL)	**2650**	**3160**	**4930**
The **highest level** of **quizartinib** in blood (ng/mL)	**82**	**148**	**283**
The **highest level** of **AC886** in blood (ng/mL)	**132**	**160**	**231**

*This means how much quizartinib and AC886 in nanograms (one thousand-millionth of a gram) were found in each milliliter of blood over time.

How was this study useful for patients and researchers?

This was the first clinical study in Japanese AML patients. It helped researchers learn about the safety of different doses of quizartinib and how the body affected its blood levels in Japanese people with relapsed or refractory AML. Oral quizartinib was approved for use in Japan in June 2019.

Findings from this study may be used to determine the recommended doses for future quizartinib studies. 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 websites:

- www.clinicaltrials.gov: Use the NCT identifier NCT02675478 in the search field.
- www.clinicaltrials.jp: Use the JapicCTI identifier JapicCTI-163142 in the search field.

Please remember that the results on these websites 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, Dose Escalation Study of Quizartinib, an Oral FLT3 Inhibitor, in Japanese 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

For any queries related to the summary

Date of this summary: 15 March 2021

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