



Daiichi-Sankyo

## Clinical Results Summary

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

**Protocol number:** AC220-A-J102

**Thank You!**



Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for quizartinib, also known as AC220. Each participant helped to advance medical research for people with a type of blood cancer called 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 acute myeloid leukemia, or 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 bloodstream and circulate in the blood, and go to different parts of the body.


Treatment for AML is usually given in 2 stages:

- Induction stage – to kill the cancer cells in the blood and bone marrow and allow normal cells to grow in the bone marrow and blood circulating throughout the body.
- Consolidation stage – to lower the risk of the cancer coming back. Treatment options include chemotherapy, or in certain cases the patient may undergo stem cell transplant.

Chemotherapy uses medicines to kill cancer cells. In AML, the patients have chemotherapy through a drip into a vein. Stem cell transplant attempts to remove the cancerous blood forming cells from the bone marrow and replace them with healthy cells taken, in most 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 of quizartinib and how the body affected blood levels (pharmacokinetics) of quizartinib and its breakdown product AC886, when taken with standard induction and consolidation therapy, in Japanese people newly diagnosed with AML.

## Treatments given in this study




**Quizartinib**

An investigational drug being tested for the treatment of AML



**Chemotherapy treatment**

**Induction therapy**  
Cytarabine  
Daunorubicin OR Idarubicin



**Consolidation therapy**  
Cytarabine only

## Main purposes of this study

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

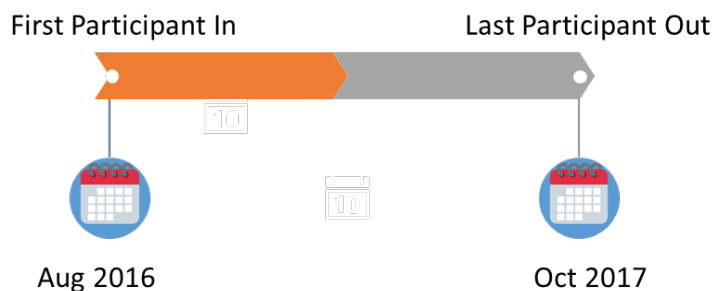


What side effects did the participants develop when quizartinib was given along with standard induction and consolidation therapy?



What were the levels of quizartinib and its breakdown product AC886 in the blood of participants when quizartinib was given along with standard induction and consolidation therapy?

## How long was this study?



The study was designed in such a way that an individual participant could be in the study for up to 6 months.

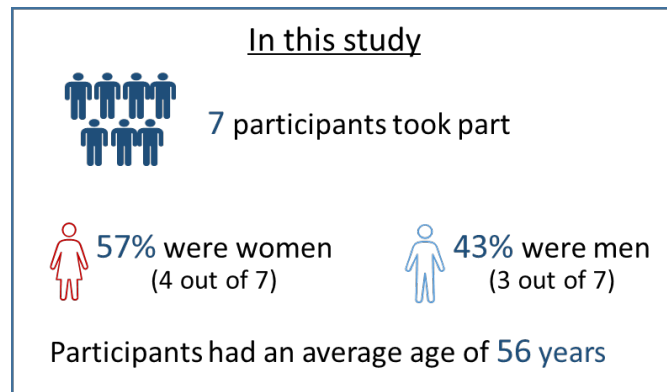
This study was completed as planned. The first participant was enrolled in the study in August 2016. The results were collected up to October 2017 and a study report was created. This summary is based on that report.

## Who was in this study?

This study included 7 participants from Japan.

Participants could take part in this study if they:

- were 20 to 75 years old
- were newly diagnosed with AML
- could take quizartinib by mouth
- were able to stay in the hospital during the safety assessment period
- 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
- did not receive any previous treatment for AML
- did not have major heart problems
- did not have any other diseases or abnormal lab tests that could prevent them from taking part in 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 Phase 1 study helped researchers understand what happens to quizartinib in combination of standard induction and consolidation chemotherapy in patients with newly diagnosed AML and if there are any side effects.

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

Participants took quizartinib tablets once every morning for 14 days during 1 cycle of treatment (which lasted 28 days). This cycle of treatment could be repeated until the study treatment had to be stopped due to any of the reasons listed on the right.

The treatment during this study was given to participants in 2 stages: the induction stage and the consolidation stage.

Participants could receive up to 2 cycles of treatment during the induction stage and 4 cycles of treatment during the consolidation stage.

Researchers started by giving 20 mg of quizartinib to the first group of participants (Group 1). Once the researchers considered this dose of quizartinib safe, the next group of participants (Group 2) received 40 mg of quizartinib.



#### **Reasons for stopping study treatment**

- *Cancer worsening*
- *Intolerable or serious side effects or changes in electrical activity in the heart (Electrocardiogram QT prolonged)*
- *Need to reduce the dose a second time*
- *Need to receive stem cell transplant*
- *Poorly following treatment procedure or failure to visit study center as scheduled for the study*
- *Did not show response to treatment after induction stage*
- *Participant's request to withdraw from the study treatment.*

## **Induction stage**

In the induction stage, quizartinib was given with standard induction chemotherapy (cytarabine and daunorubicin, or idarubicin) for up to 2 cycles. The participants who responded with either complete remission (CR) or complete remission with incomplete platelet recovery (CRp) or complete remission with incomplete hematological recovery (CRi)\* at the end of the induction stage could proceed to the consolidation stage.

**\*CR:** means less than 5% (5 out of 100) cells in their 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 for any transfusion.

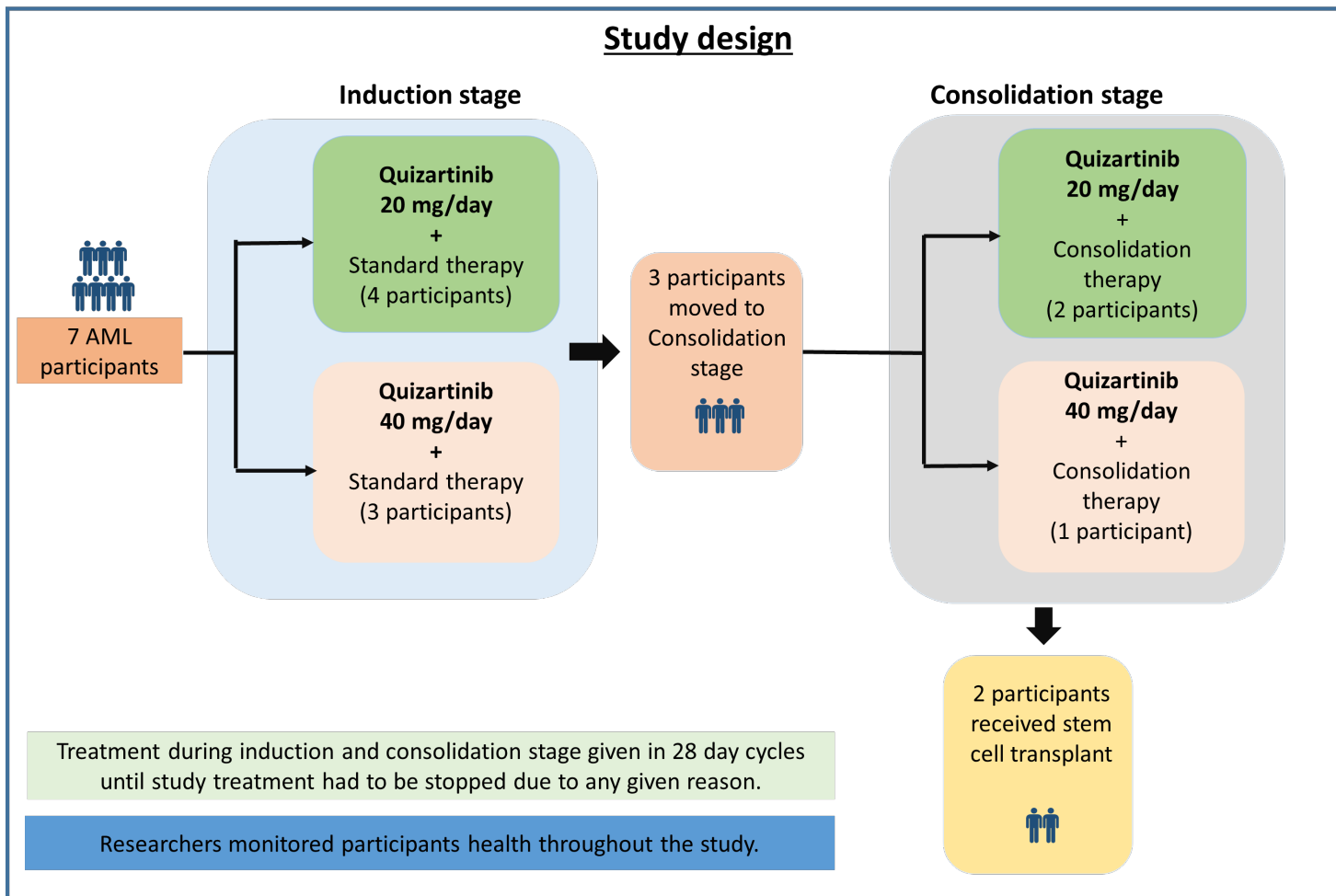
**CRp:** means less than 5% of cells in the participant's bone marrow were cancer cells, with incomplete recovery of platelets.

**CRi:** means 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 participants may or may not have needed a blood or platelet transfusion.

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

## **Consolidation stage**

In the consolidation stage, quizartinib was given with consolidation chemotherapy (cytarabine only) for up to 4 cycles. Participants continued on to the consolidation stage only if they achieved CR, CRp or CRi. The participants who achieved CR, CRp or CRi after induction stage or later could go on to receive a stem cell transplant.



## 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 when quizartinib was given along with standard induction and consolidation therapy?

The study was also trying to identify if there were any Dose Limiting Toxicities (DLTs)\* caused by quizartinib.

\*DLTs are defined as certain severe medical toxicities caused by quizartinib. The time period during which DLTs were measured was from Day 1 of participants taking their first quizartinib tablet to Day 42 of the last cycle of quizartinib in the induction stage, or the day before participants moved to the consolidation stage, whichever came earlier.

Side effects are medical problems (this may range from something mild such as feeling tired or something more severe like a severe infection) that happened during the study. This section provides a summary of side effects related to quizartinib.

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

Side effects other than those related to quizartinib 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?**

In this study, side effects were monitored for all participants who took part in this study. There were no deaths reported related to quizartinib.















During the induction stage, 1 out of 3 (33%) participants in Group 2 (40 mg) experienced a serious side effect of blood infection due to *Staphylococcus aureus*. *Staphylococcus aureus* is a type of bacteria. No participant in Group 1 (20 mg) had serious side effects.

During the consolidation stage, no participants reported any serious side effects.

### **How many participants had side effects?**

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































All 7 (100%) participants reported side effects related to quizartinib. The most common side effects, which happened in at least 50% (1 out of 2) of participants in any group during the **induction stage**, are presented below.

Group 1 (20 mg) Percentage (number of participants)			Group 2 (40 mg) Percentage (number of participants)	
 100% (4 of 4)	<b>Side effects</b>	100% (3 of 3)		
 50% (2 of 4)	Abnormal increase in GGT (one of the tests of how the liver is functioning)	33% (1 of 3)		
 25% (1 of 4)	Abnormally low number of neutrophils accompanied by fever	67% (2 of 3)		
 0%	Changes in electrical activity in the heart <sup>a</sup> (Electrocardiogram QT prolonged)	67% (2 of 3)		
 50% (2 of 4)	Low hemoglobin levels in blood	0%		
 50% (2 of 4)	Stomach pain	0%		
 50% (2 of 4)	Sore and inflamed mouth	0%		

a: Detected using an ECG of the heart



The side effects that occurred during the **consolidation stage** are presented below.

Group 1 (20 mg) Percentage (number of participants)			Group 2 (40 mg) Percentage (number of participants)	
	100% (2 of 2)	<b>Side effects</b>	100% (1 of 1)	
	50% (1 of 2)	Abnormal increase in ALT (one of the tests of how the liver is functioning)	0%	
	100% (2 of 2)	Abnormally low number of neutrophils accompanied by fever	100% (1 of 1)	
	50% (1 of 2)	Abnormally low number of platelets	100% (1 of 1)	
	50% (1 of 2)	Altered taste	0%	
	0%	Changes in electrical activity in the heart <sup>a</sup> (Electrocardiogram QT prolonged)	100% (1 of 1)	
	50% (1 of 2)	Diarrhea	0%	
	50% (1 of 2)	Feeling sick (the desire to vomit)	0%	
	0%	Lung infection	100% (1 of 1)	
	50% (1 of 2)	Lower number of white blood cells	100% (1 of 1)	
	0%	Raised red bumps on the skin	100% (1 of 1)	
	50% (1 of 2)	Rash	0%	
	50% (1 of 2)	Skin infection	0%	
	50% (1 of 2)	Sore and inflamed mouth	0%	
	50% (1 of 2)	Swelling of the feet and hands	0%	

a: Detected using an ECG of the heart

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

No participant stopped treatment due to side effects.



What were the levels of quizartinib and its breakdown product AC886 in the blood of participants when quizartinib was given along with standard induction and consolidation therapy?

To answer this question, researchers measured the following:

- Total level of quizartinib and AC886 in the participants' blood over 24 hours after taking quizartinib.
- Highest level of quizartinib and AC886 in the participants' blood after taking quizartinib.

The average results of these measurements are presented below. Total level of quizartinib and AC886 in the participants' blood is measured in ng·hr/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.

### Levels of quizartinib in the blood

	Day 21 of Induction stage	
	Group 1 (20 mg)	Group 2 (40 mg)
<b>Total level over 24 hours</b> (ng·hr/mL)	1210	3280
<b>Highest level</b> (ng/mL)	73	223

### Levels of AC886 in the blood

	Day 21 of Induction stage	
	Group 1 (20 mg)	Group 2 (40 mg)
<b>Total level over 24 hours</b> (ng•hr/mL)	1990	5520
<b>Highest level</b> (ng/mL)	99	268

\*This means the total levels of quizartinib and AC886 in nanogram (one thousand-millionth of a gram) found in each milliliter of blood up to 24 hours after taking quizartinib tablet.

## How was this study useful for patients and researchers?

This study helped researchers learn about the safety and the blood levels of quizartinib and AC886 in Japanese patients newly diagnosed with AML. There were no DLTs caused by quizartinib. Therefore the doses of 20 mg and 40 mg quizartinib, in combination with induction and consolidation therapy, were considered to be safe by the researchers. Findings from this study also helped to determine whether Japanese patients could participate in another larger global study of the effects of quizartinib in patients with newly diagnosed AML. Other studies of quizartinib are still 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](http://www.clinicaltrials.gov): Use the NCT identifier NCT02834390 in the search field.



<https://www.clinicaltrials.jp>: Use the Registry identifier JapicCTI-163309 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 1b Clinical Study of Quizartinib (AC220)–Evaluation of the Safety and Pharmacokinetics of Quizartinib in Combination with Standard Induction and Consolidation Therapy in Japanese Patients with Newly Diagnosed Acute Myeloid Leukemia

**Sponsor:** Daiichi Sankyo, Inc.

**Sponsor contact information:**

211 Mount Airy Road, Basking Ridge, NJ 07920

**Email:** [CTRInfo@dsi.com](mailto:CTRInfo@dsi.com)

**Phone number:** 1-908-992-6640

**Date of this summary:** 04 June 2021

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