Daiichi-Sankyo

# Clinical Results Summary

# A clinical study to learn about the safety of quizartinib in combination with standard chemotherapy in people with a type of blood cancer called acute myeloid leukemia

**Protocol number:** 2689-CL-0005

**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 affected with a type of blood cancer, called newly identified 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 were newly diagnosed with AML and did not receive any previous treatment for 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.

The main treatment for AML is chemotherapy. Chemotherapy uses medicines to kill cancer cells or to 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. This procedure removes the cancerous blood-forming cells from the bone marrow and replaces them with healthy cells taken, in most of the cases, from another healthy person (donor). The new cells can multiply and produce healthy cells.

People with AML may or may not 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 treatment, and is likely to come back even after treatment. Quizartinib is designed to work against AML cells with this genetic mutation.

In this Phase 1 study, researchers wanted to see how safe quizartinib was at treating people newly diagnosed with FLT3-ITD positive or negative AML when given along with the standard chemotherapy. Phase 1 studies are done to find out the safety of a new study treatment, how it works, and what happens to the study treatment in the body of a a small number of participants.

## Treatments given in this study

**Quizartinib**
(Investigational drug)

An investigational drug being tested for the treatment of newly diagnosed AML participants

**Standard Chemotherapy**
(Approved drugs)

**Induction therapy:** daunorubicin + cytarabine
**Consolidation therapy:** high-dose cytarabine (HiDAC)

## Main purposes of this study

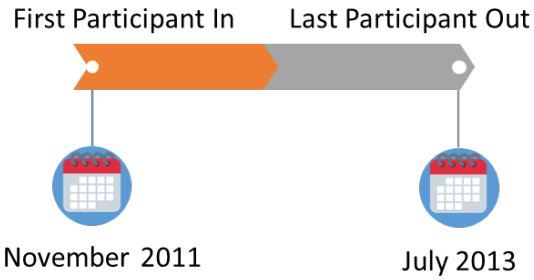
The main questions the researchers wanted to answer in this study were:

How many participants had side effects during the study?

What were the Dose-Limiting Toxicities caused by quizartinib in combination with standard chemotherapy?

*Dose-limiting toxicities are defined as certain severe medical toxicities caused by quizartinib in combination with standard chemotherapy.*

# How long was this study?




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

The first participant entered the study in November 2011. The sponsor ended this study early for administrative and resource issues which were not related to any safety or effects of quizartinib.

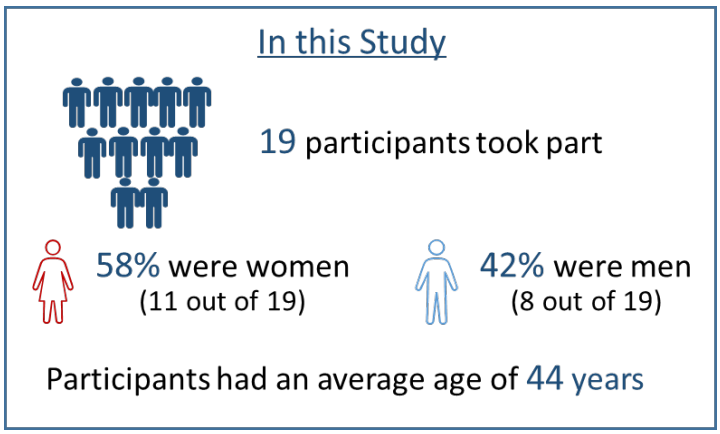
The study ended in July 2013 and a study report was created. This summary is based on that report.

# Who was in this study?

This study included 19 participants from the United States.

Participants could take part in this study if they:

- were 18 to 60 years old,
- were newly diagnosed with AML,
- did not receive any previous treatment for AML,
- had normal kidney, liver, and blood clotting parameters, and
- 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.




# What happened during this study?

This study was "open label". This means that both the researchers and the participants knew which treatment was given to which participants. Participants took quizartinib oral solution along with standard chemotherapy as an injection. The study treatment was given to participants in 2 phases: the induction phase followed by the consolidation phase.

## Induction phase

The aim of the induction phase is to clear the participants' blood of AML. In the induction phase, quizartinib was given with standard chemotherapy (daunorubicin and cytarabine) for up to 2 cycles. Participants took quizartinib tablets once every day for 7 or 14 days during 1 cycle of treatment (which lasted 42 days). The participants who showed either complete remission (CR) or complete remission with incomplete hematological recovery (CRi) at the end of the induction phase could proceed to the consolidation phase.

CR and CRi were defined as:

- **Complete remission** which is also called **"CR":** CR meant less than 5% (5 out of 100) cells in 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 blood or platelet transfusion.

- **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, OR incomplete recovery of platelets. The participants may or may not have needed blood or platelet transfusion.

**Neutrophils are a type of white blood cell that fights bacteria. Platelets are a type of blood cell that helps in preventing/stopping bleeding.*

## Consolidation phase

The aim of the consolidation phase is to maintain the response the participant achieved at the end of the induction phase. In the consolidation phase, participants took quizartinib tablets once every morning for 7 or 14 days during 1 cycle of treatment (which lasted 21 days). Quizartinib was given with standard chemotherapy (high-dose cytarabine) for up to 3 cycles or until participants could go on to receive a stem cell transplant. Participants continued to the consolidation phase only if their blood cancer disappeared.

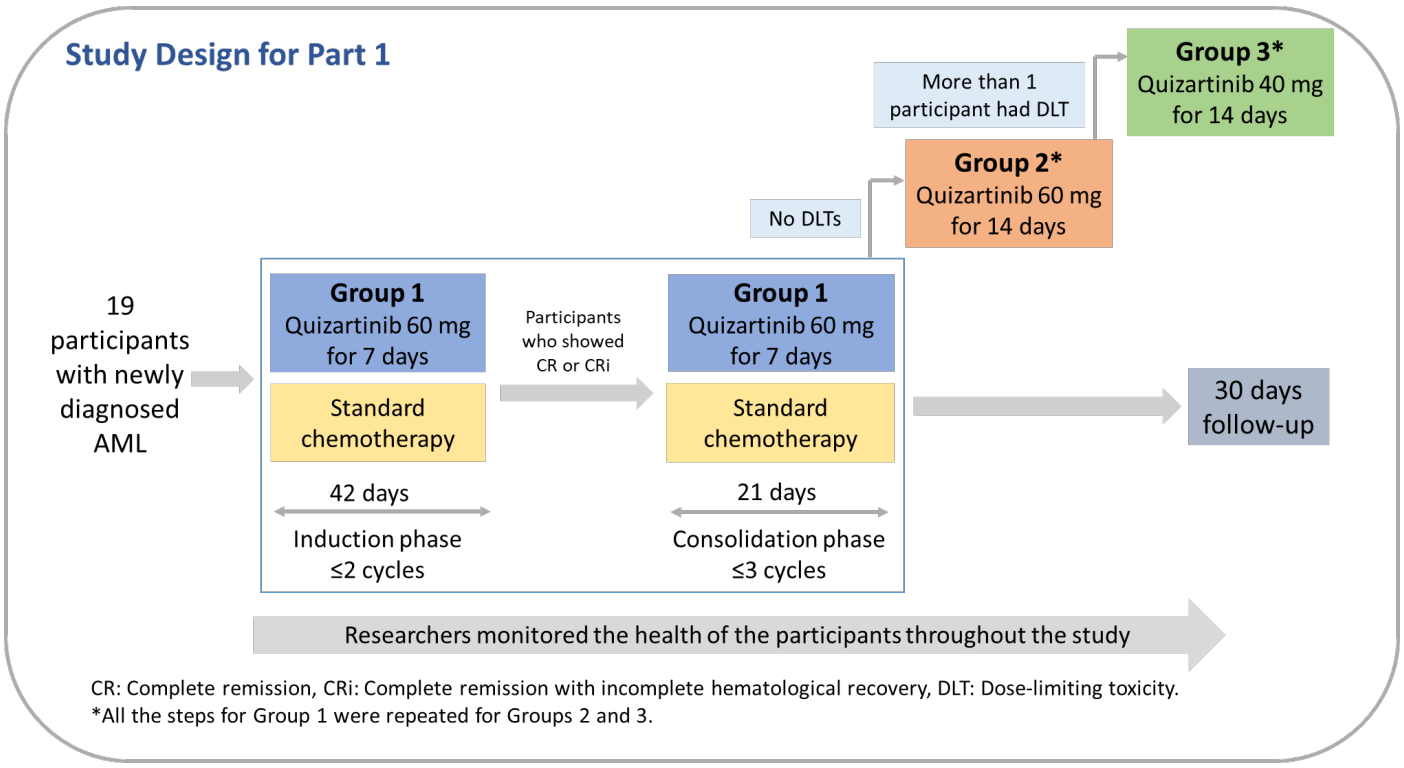
This study was divided into 2 parts.

## Part 1

During Part 1, researchers started by giving participants 60 milligrams (mg) of quizartinib for 7 days (Group 1). Once the researchers considered this dose of quizartinib safe, the next group of participants received 60 mg of quizartinib for 14 days (Group 2). At this dose level and schedule (60 mg for 14 days), researchers noted some dose-limiting toxicities (DLTs), so the next group of participants received a lower dose of 40 mg for 14 days (Group 3). This dose was identified as the highest dose of quizartinib that could be safely given to participants, therefore it was selected for further research in Part 2 of the study.

## 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 Part 1, researchers decided that 40 mg dose for 14 days was the maximum dose to be taken in further planned studies.




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

## What were the key results of this study?

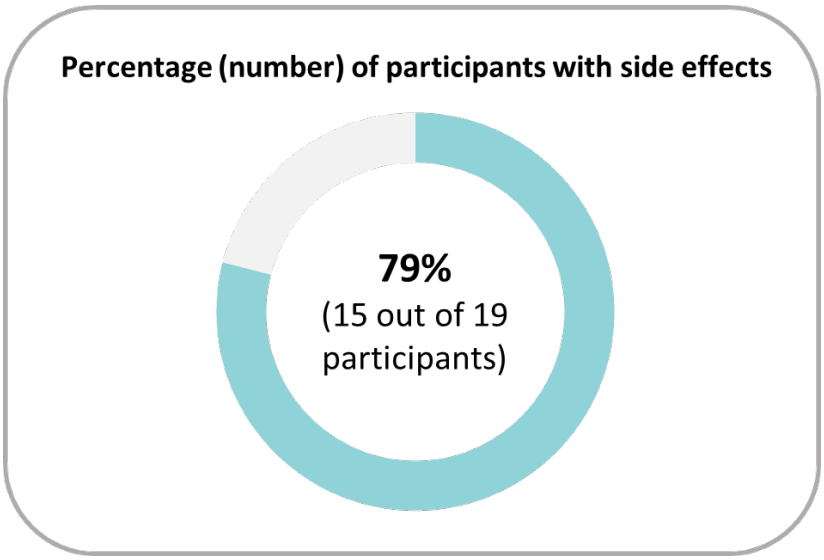
Key results from this study are shown for the total group of participants as average results. This summary does not show the results from each individual participant. An individual participant's results could be different from the total group of participants. A full list of the questions the researchers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

### How many participants had side effects 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. Detailed information about side effects

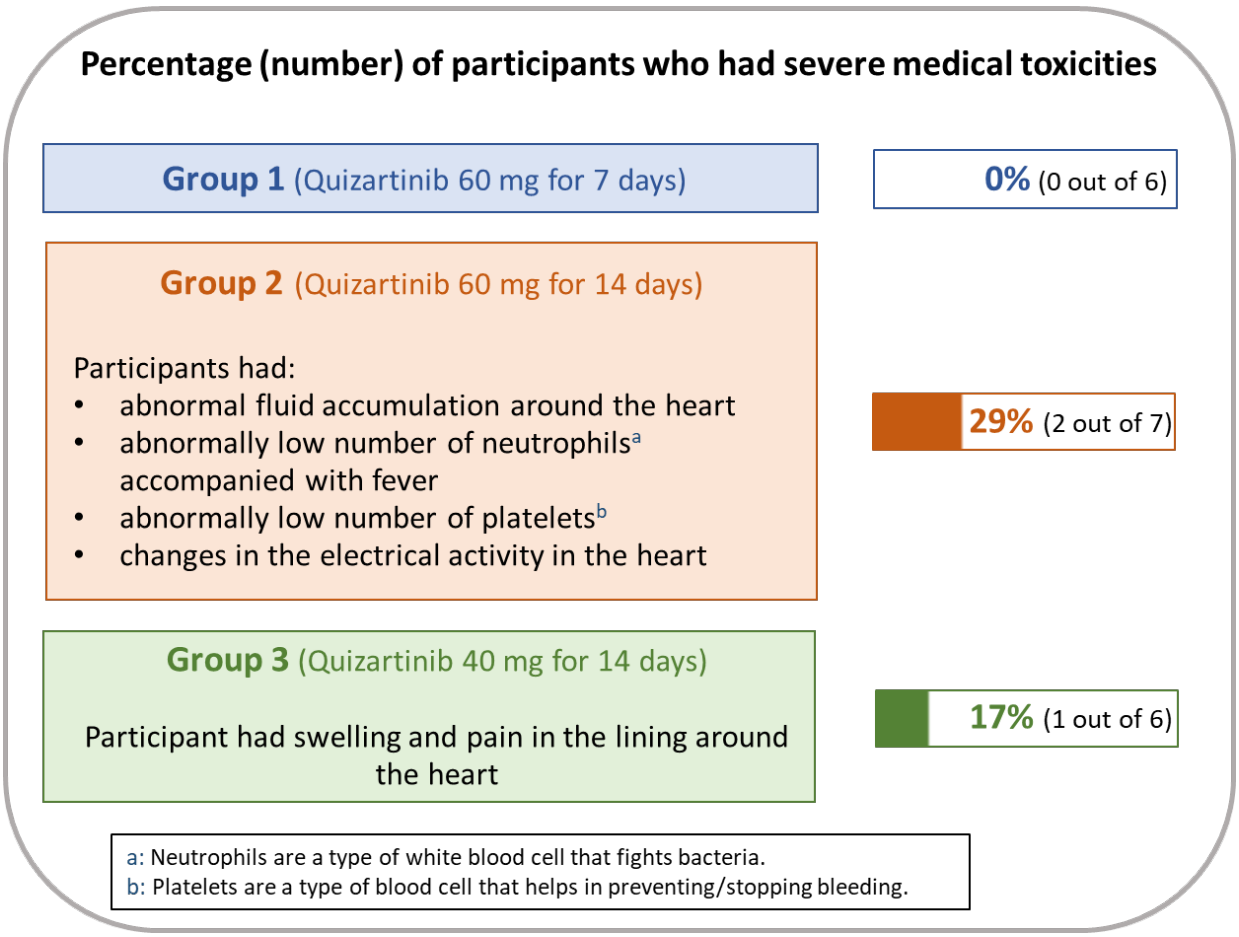
reported by participants is presented in the section 'What side effects did the participants develop during the study?'

During the study, 79% (15 out of 19) participants had side effects.




## What were the Dose-Limiting Toxicities caused by quizartinib in combination with standard chemotherapy?

The number of dose-limiting toxicities helped researchers decide whether the given dose of quizartinib in combination with standard chemotherapy was safe, and decide the dose of quizartinib that could be given to the next group of participants.



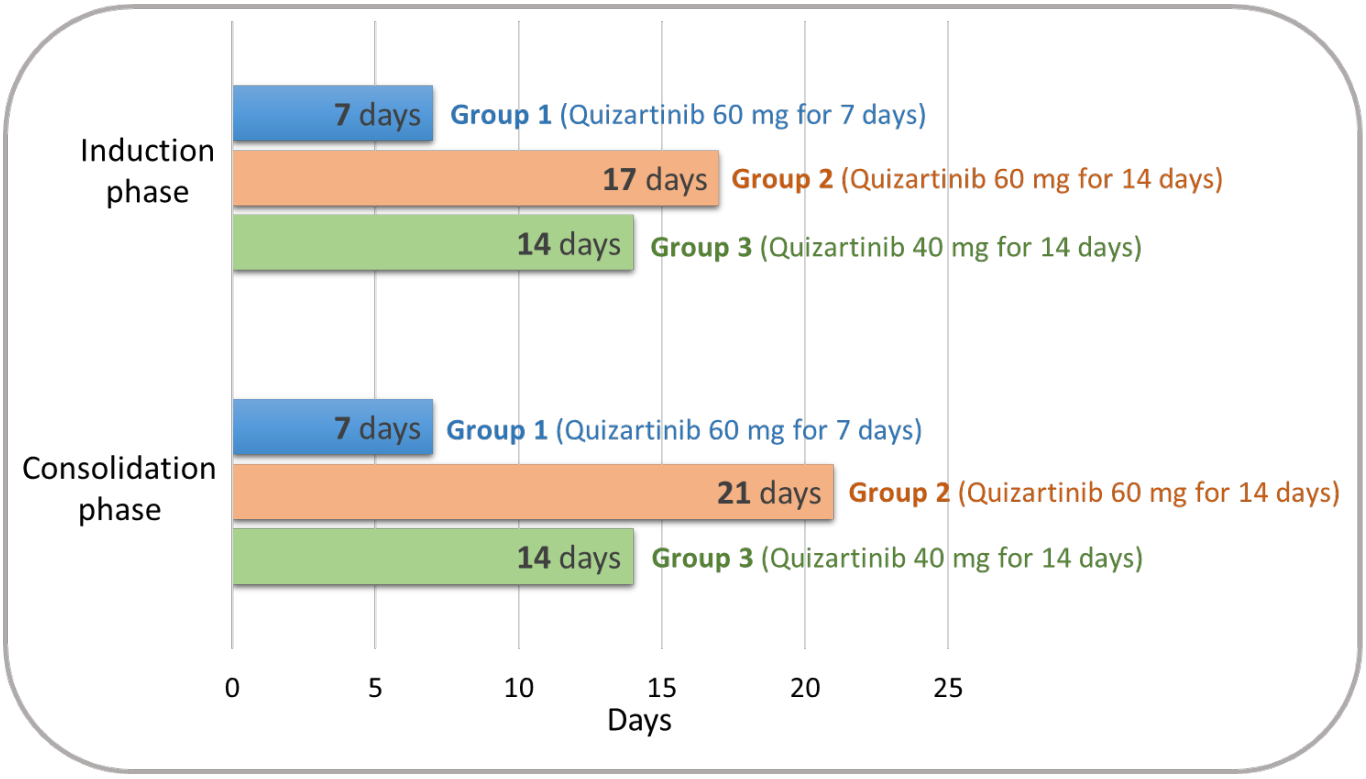

## What side effects did the study participants develop during the study?

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 long did the participants receive treatment during the study?

Participants in Group 2 were in the study longer than the participants in Group 1 or Group 3. The next figure shows the median duration for which the participants in any of the groups received quizartinib. Median means the midpoint value for a group. For example, for the participants in Group 1, the duration of the treatment for half of them was less than 7 days, and for the other half, it was more.



## How many participants had serious side effects?

In this study, side effects were monitored for 19 participants. A total of 16% (3 out of 19) participants had serious side effects related to quizartinib.

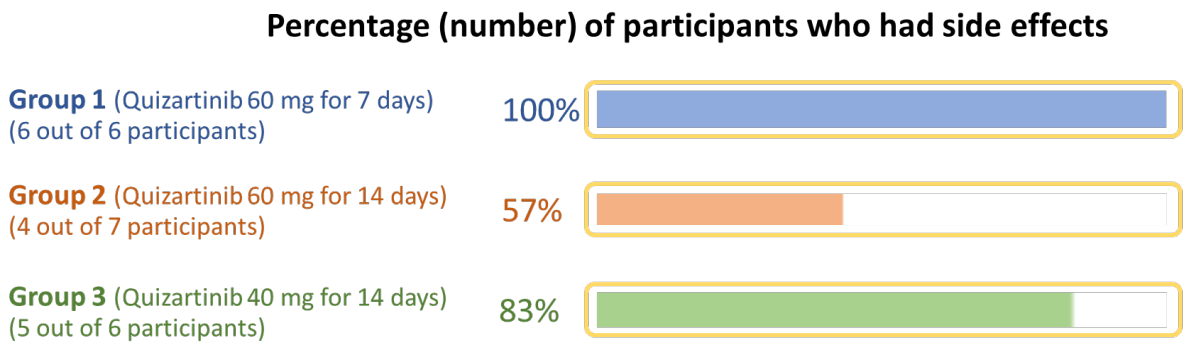
- **Group 1 (Quizartinib 60 mg for 7 days):** 33% (2 out of 6) participants had serious side effects.
  1 participant had a side effect of abnormally low number of neutrophils accompanied with fever. The other participant had a side effect of liver infection.
- **Group 2 (Quizartinib 60 mg for 14 days):** None of the 7 participants in this group had serious side effects.
- **Group 3 (Quizartinib 40 mg for 14 days):** 17% (1 out of 6) participants had serious side effects of inflammation in the membrane/coat surrounding the heart and feeling sick to the stomach.

There were no deaths due to quizartinib.

## How many participants had side effects?

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

79% (15 out of 19) of participants reported side effects related to quizartinib.



The most common side effects, which happened in at least 20% of the participants in any group, are presented below.

| Side effects | Group 1 (out of 6 participants) | Group 2 (out of 7 participants) | Group 3 (out of 6 participants) |
|---|---|---|---|
| Abnormally low number of neutrophils[a] | 33% (2) | 14% (1) | 17% (1) |
| Abnormally low number of neutrophils[a] accompanied with fever | 33% (2) | 29% (2) | 17% (1) |
| Abnormally low number of platelets[b] | 33% (2) | 14% (1) | 17% (1) |
| Feeling sick to the stomach | 67% (4) | 43% (3) | 33% (2) |
| Feeling tired | 17% (1) | 14% (1) | 33% (2) |
| Fever | 33% (2) | 0 | 33% (2) |
| Loose stools | 17% (1) | 29% (2) | 50% (3) |
| Low hemoglobin levels in the blood | 33% (2) | 29% (2) | 17% (1) |

a: Neutrophils are a type of white blood cell that fights bacteria.
b: Platelets are a type of blood cell that helps in preventing/stopping bleeding.

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

Due to side effects, 11% (2 out of 19) of participants stopped treatment early. These were redness, swelling, and pain on the hands and feet which is associated with tingling sensation in **Group 2 (Quizartinib 60 mg for 14 days)**; and inflammation in the membrane/coat surrounding the heart and feeling sick to the stomach in **Group 3 (Quizartinib 40 mg for 14 days)**. The side effect of inflammation in the membrane/coat surrounding the heart was a Dose-Limiting Toxicity.

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

This study helped researchers learn about a safe dose of quizartinib in patients with newly diagnosed AML who had not received any previous treatment for AML.

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 websites:

- www.clinicaltrials.gov: Use the NCT identifier NCT01390337 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 Study of AC220 in Combination with Induction and Consolidation Chemotherapy in Patients with Newly Diagnosed Acute Myeloid Leukemia (AML)

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