



Daiichi-Sankyo

## Clinical Results Summary

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

**Protocol number:** 2689-CL-2004

**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 acute myeloid leukemia, or AML. The participants in this study had FLT3-ITD positive refractory or relapsed AML that either:

- did not respond to their second AML treatment (known as refractory AML), or
- did respond and were free of disease but then their AML came back after their second AML treatment or stem cell transplant (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 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 positive 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 effective and safe quizartinib is at treating people with refractory or relapsed FLT3-ITD positive AML.

## Treatment given in this study



### Quizartinib

An investigational treatment being tested for the treatment of relapsed or refractory AML participants who tested positive for FLT3-ITD

## Main purposes of this study

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



How many participants achieved composite complete remission to treatment with quizartinib?

**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.



How many participants showed abnormal changes in the electrical activity of heart (Electrocardiogram QT prolonged) after treatment with quizartinib?

## Other purposes of this study

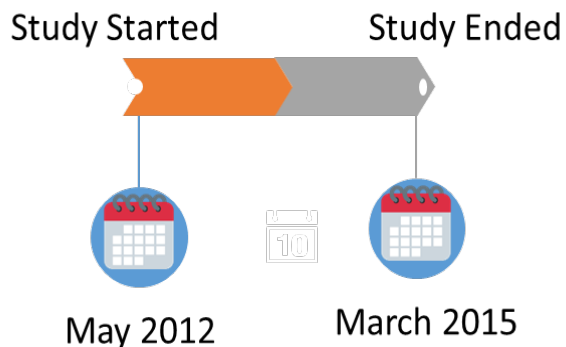
Researchers also wanted to answer the following questions:

- How long did AML participants live after initiating treatment with quizartinib until they died due to any cause? This is also called '**Overall Survival**'.
- For participants who achieved composite complete remission or partial remission\* to quizartinib treatment, how long did the effect last? This is also called '**Duration of Remission**'.
- What side effects did the participants develop during the study?

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

\*Partial remission was defined as disappearance of at least 50% of the participant's blood cancer cells after treatment.

## How long was this study?



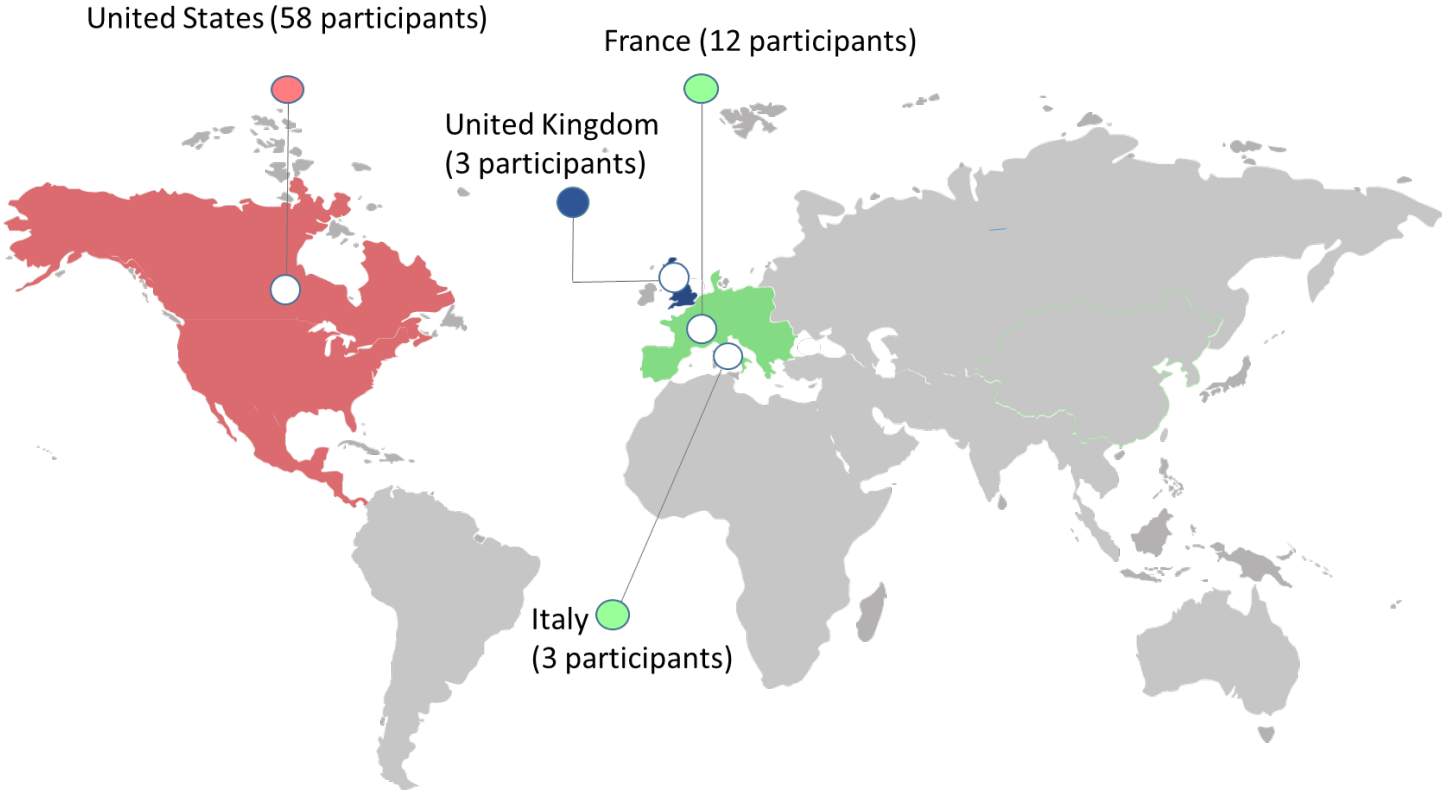
The study was designed in such a way that the participants could continue in it as long as they benefited from the treatment and their AML did not get worse, and they did not have any serious side effects. A serious side effect could have caused a participant to discontinue their treatment with quizartinib.

The study was completed as planned. The study started in May 2012 and ended in March 2015 and a study report was created. This summary is based on that report.

# Who was in this study?

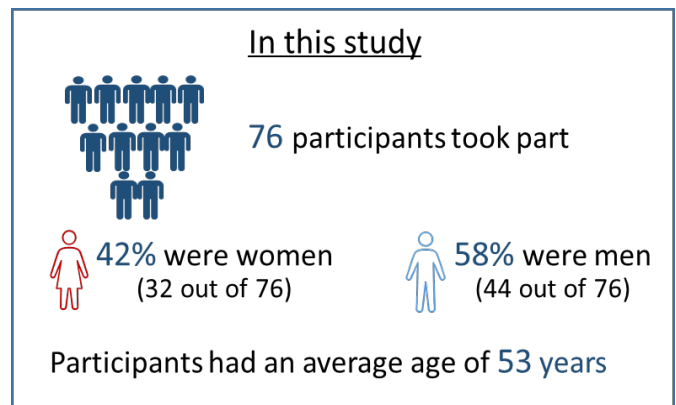
This study included 76 participants from the following 4 countries:

## Participants by country



Participants could take part in this study if they:

- were diagnosed with AML or myelodysplastic syndrome (another type of blood cancer) that progressed to AML,
- tested positive for the FLT3-ITD mutation,
- were aged 18 years or older,
- did not respond to their second AML treatment, or did respond and were free of disease but then their AML came back after receiving their second AML treatment or stem cell transplant,
- 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 have any major heart problems such as an irregular heart rhythm or family history of the same or chest pain,
- 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 2 study. In Phase 2 studies, the study treatment is given to a small number of participants with the disease condition to gather information about the effects of the study treatment.

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

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

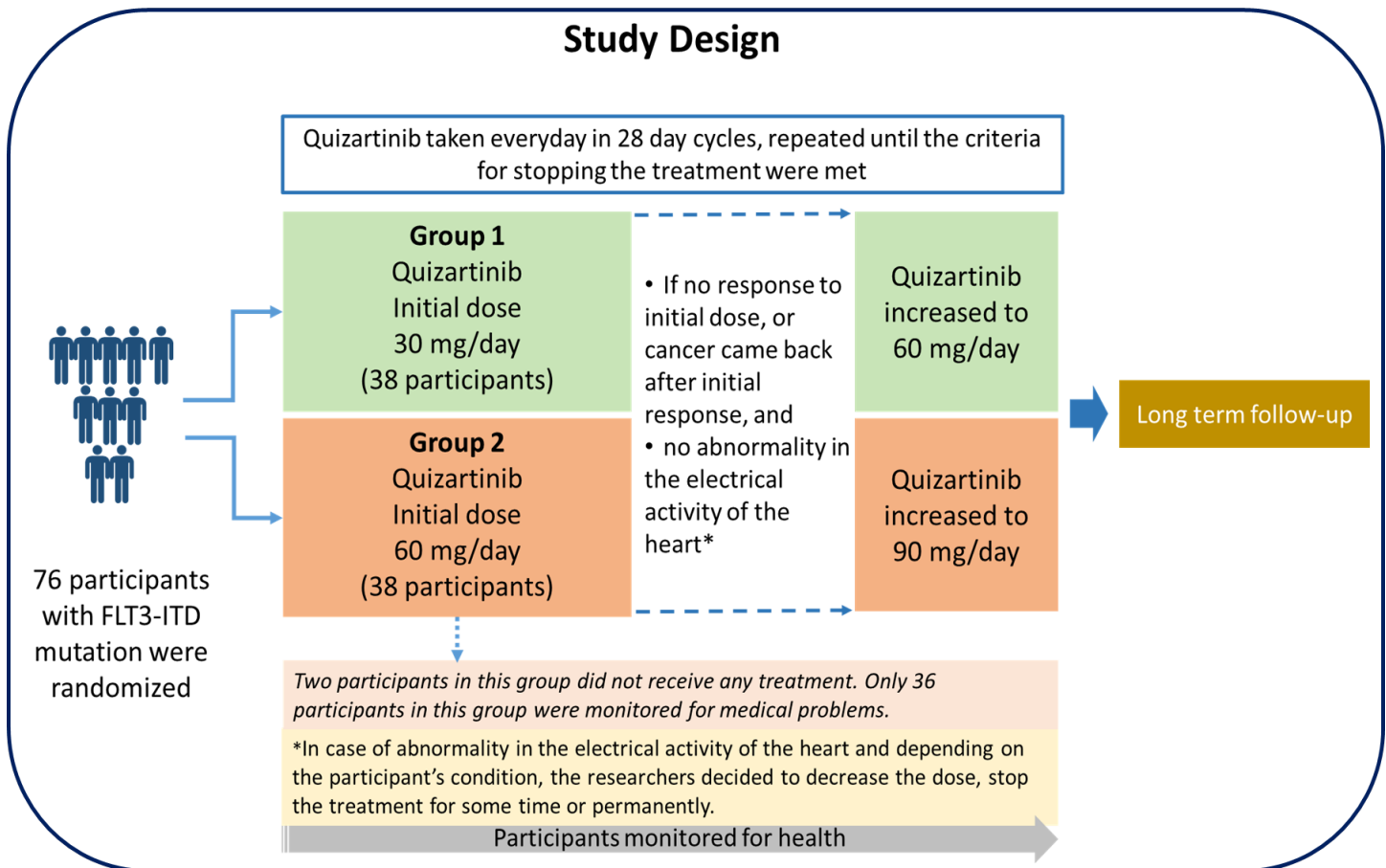
Researchers used a computer system to assign participants into two groups by a process called randomization. The system was designed to ensure that participants were equally divided into two groups:

- Group 1: participants received a starting dose of 30 milligrams/day (mg/day) of quizartinib
- Group 2: participants received a starting dose of 60 mg/day of quizartinib.

Participants took quizartinib oral solution once every morning for 28 days. This cycle of treatment could be repeated for as long as they benefited from the treatment without any serious side effects.

The 30 mg/day dose could be increased to 60 mg/day and the 60 mg/day dose could be increased to 90 mg/day in participants with no response or whose cancer came back.

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. During the long term follow-up, the participants well-being and further AML treatment were checked via a phone call every 3 months.



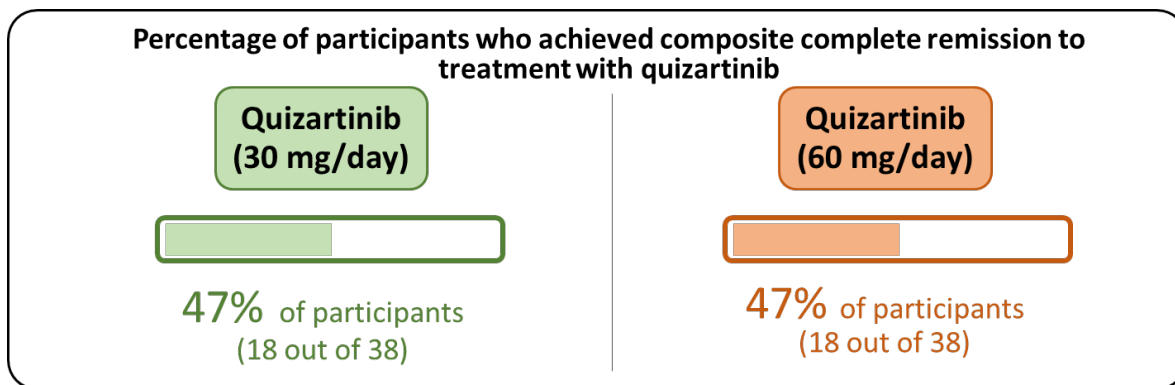
## What were the key results of this study?

Key results from this study are shown for each group of participants collectively. 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 achieved composite complete remission to treatment with quizartinib?



How many participants showed abnormal changes in the electrical activity of heart (Electrocardiogram QT prolonged) after treatment with quizartinib?

To answer this question, researchers measured the heart’s electrical activity of each participant during the study using a simple test called electrocardiogram (ECG). This test measures disruptions in the heart’s electrical activity. Researchers calculated how many participants had disruptions in their heart’s electrical activity. Researchers then categorized the participants into different levels based on their recorded value in milliseconds (msec).

Researchers reported abnormal changes in the electrical activity of heart of 2 subjects in the 60 mg/day group as serious side effects. Please refer to the section ‘How many participants had serious side effects?’ on Page 11.



**Percentage of participants who showed abnormal changes in the electrical activity of heart (Electrocardiogram QT prolonged) after treatment with quizartinib**

Level of change in the electrical activity of heart	Quizartinib (30 mg/day)	Quizartinib (60 mg/day)
Level <b>1</b> <b>Mild</b> between 450 and 480 msec	42% (16 out of 38 participants )	47% (17 out of 36 participants)
Level <b>2</b> <b>Moderate</b> between 480 and 500 msec	5% (2 out of 38 participants )	14% (5 out of 36 participants)
Level <b>3</b> <b>Severe</b> more than 500 msec	5% (2 out of 38 participants )	3% (1 out of 36 participants)

## 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 cancer or any other cause. At the end of this study, researchers found that:

- about half of the participants who started quizartinib at the 30 mg/day dose lived for at least **21 weeks**, and
- about half of the participants who started quizartinib at the 60 mg/day dose lived for at least **27 weeks**.

## For participants who achieved composite complete remission or partial remission to quizartinib treatment, how long did the effect last?

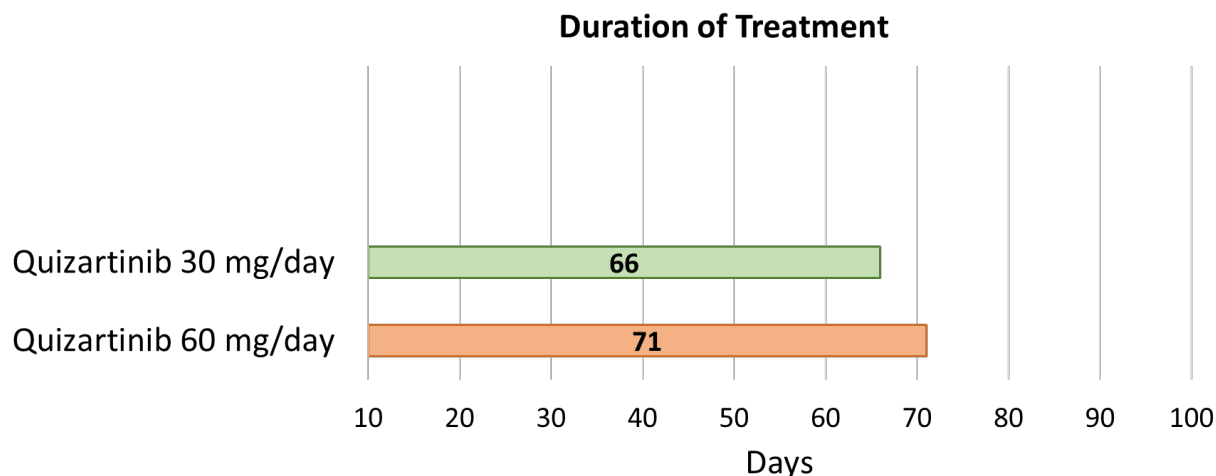
Researchers measured the time from the participants' first response to study treatment which included either composite complete remission or partial remission until their cancer came back. The definitions of these terms can be found on Pages 3 and 4 of this document.

Researchers found that:

- about half of the participants who achieved **composite complete remission** at the initial 30 mg/day dose, the effect lasted for at least **4 weeks**, and
- about half of the participants who achieved **composite complete remission** at the initial 60 mg/day dose, the effect lasted for at least **9 weeks**;
- about half of the participants who achieved **either composite complete remission or partial remission** at the initial 30 mg/day dose, the effect lasted for at least **7 weeks**, and
- about half of the participants who achieved **either composite complete remission or partial remission** at the initial 60 mg/day dose, the effect lasted for at least **9 weeks**.

## How long did the participants receive treatment during the trial?

The participants who took the quizartinib 60 mg/day starting dose were in the study longer than the participants who took the quizartinib 30 mg/day starting dose. The next figure shows the median duration for which the participants received treatment. Median means the midpoint value for a group. For example, in the group of the participants who were treated with the quizartinib 30 mg/day starting dose, the duration of the treatment for half of them was less than 66 days, and for the other half it was more.



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

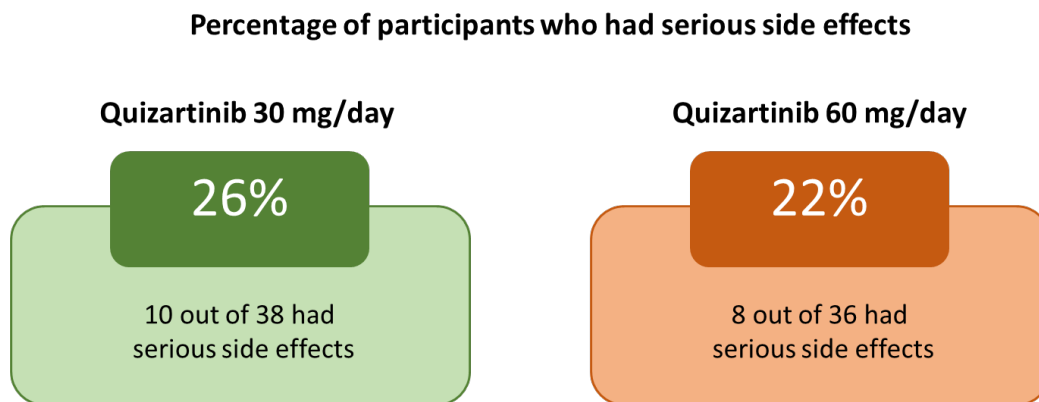
Side effects are medical problems (this may range from something mild such as feeling tired or something more severe like a severe infection or other medical problem) that happened during the study, which the study doctor thought could be related to the treatments in the study.

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 (quizartinib) 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 reported as related to quizartinib?

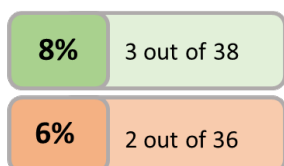
The percentage and number of participants in each group who reported at least one serious side effect related to quizartinib were:



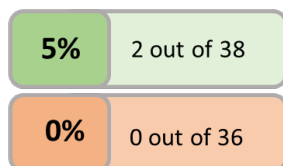
The serious side effects that occurred during the study were:

- Quizartinib 30 mg/day
- Quizartinib 60 mg/day

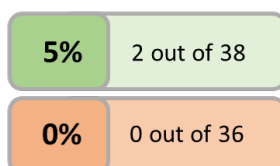
**Abnormally low number of neutrophils accompanied by fever**



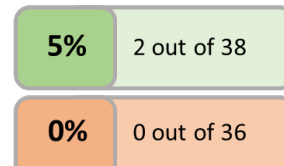
**Abnormally low number of platelets**



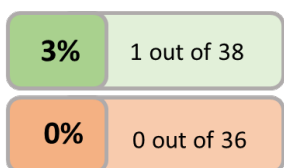
**Abnormal fluid accumulation around the heart**



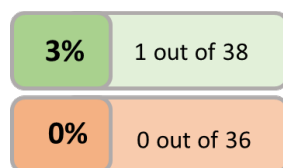
**Bleeding in the digestive tract**



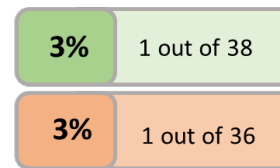
**Low hemoglobin levels in blood**



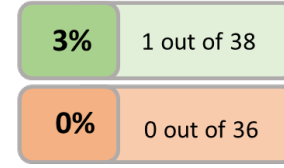
**Inflammation of the heart's covering**



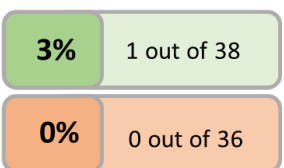
**Diarrhea**



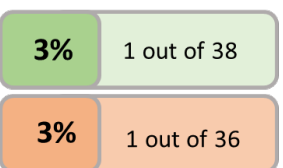
**Ulcer of esophagus**



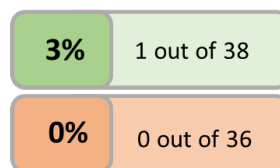
**Bleeding in lower part of large intestine**



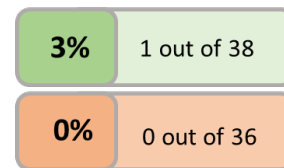
**Rise in body temperature**



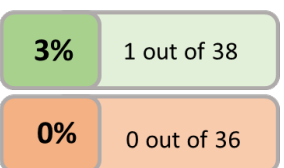
**Fever**



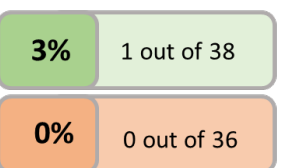
**Serious infection of blood due to low number of neutrophils**



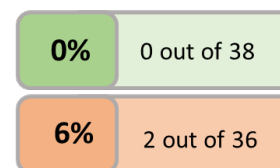
**Lung infection**



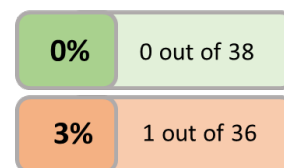
**Abnormal fluid accumulation around the lungs**



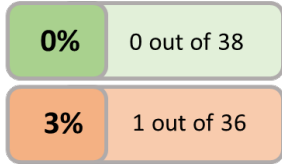
**Changes in electrical activity in the heart (Electrocardiogram QT prolonged)**



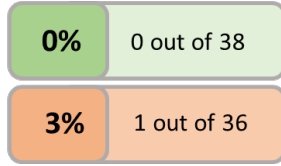
**An irregular and very rapid heart rate**



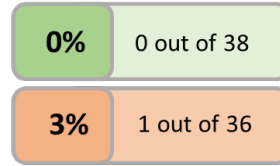
**Ulcer in the stomach**



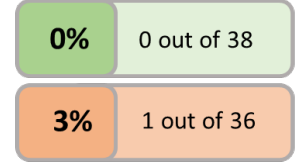
**Stroke to the intestine**



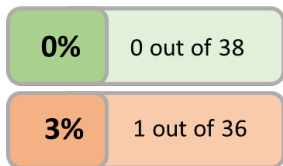
**Feeling sick  
(the desire to vomit)**



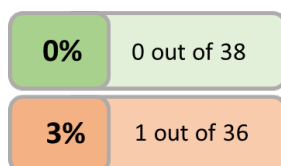
**Vomiting**



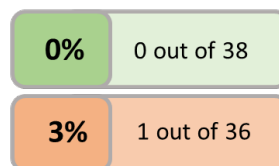
**Shock due to very low blood  
pressure caused by infection**



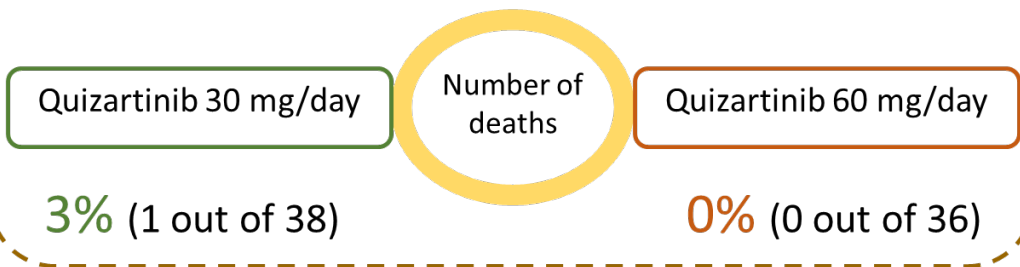
**Abnormal increase in ALT  
(one of the tests of how  
the liver is functioning)**



**Shock due to low blood  
supply to body tissues**



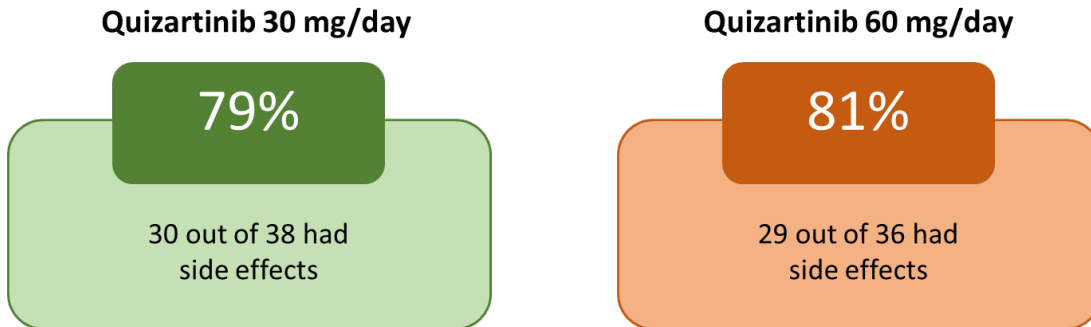
In this study, one death was reported as possibly related to quizartinib. The reason was abnormal accumulation of fluid around the heart and lungs.



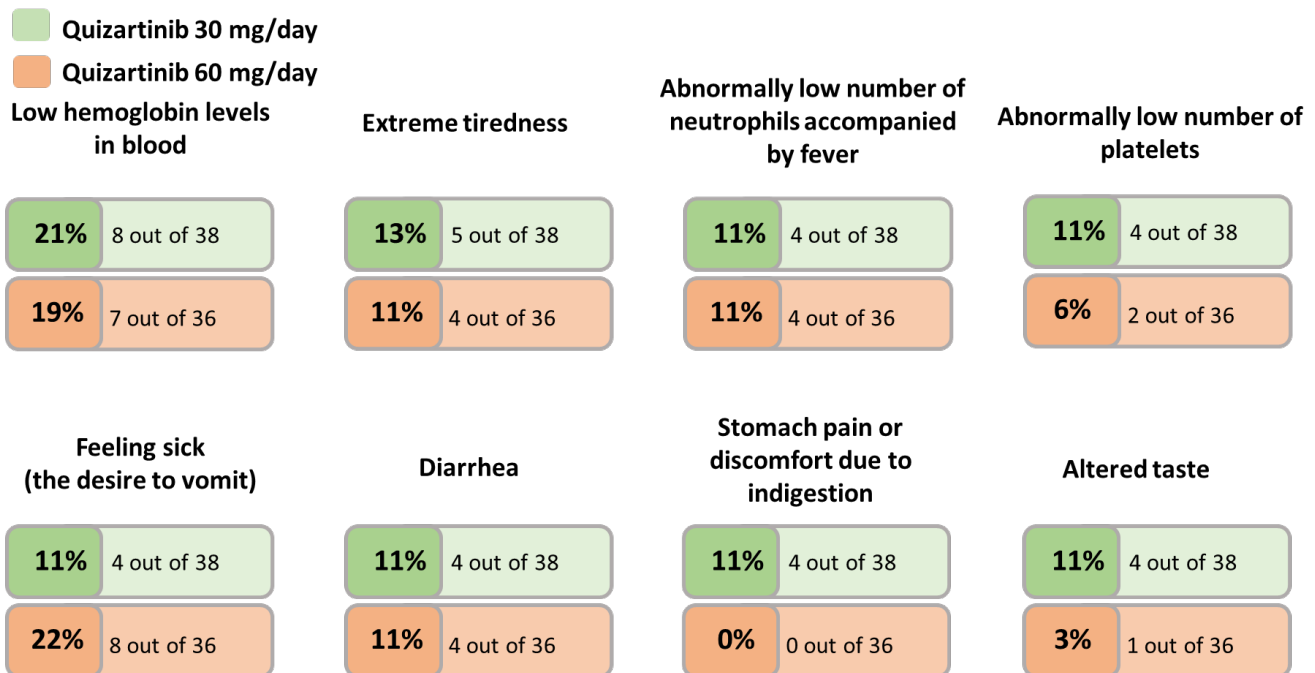
## How many participants had side effects reported as related to quizartinib?

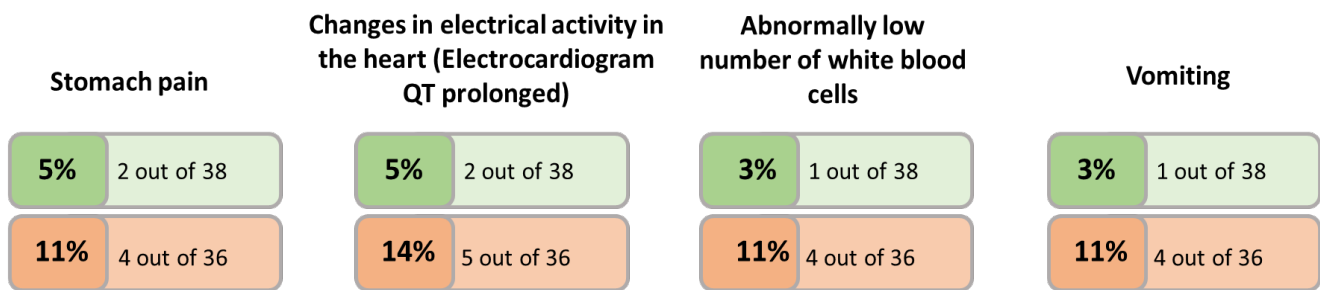
Side effects reported, both serious and non-serious, that were related to quizartinib are presented in this section.

### Percentage of participants who had side effects



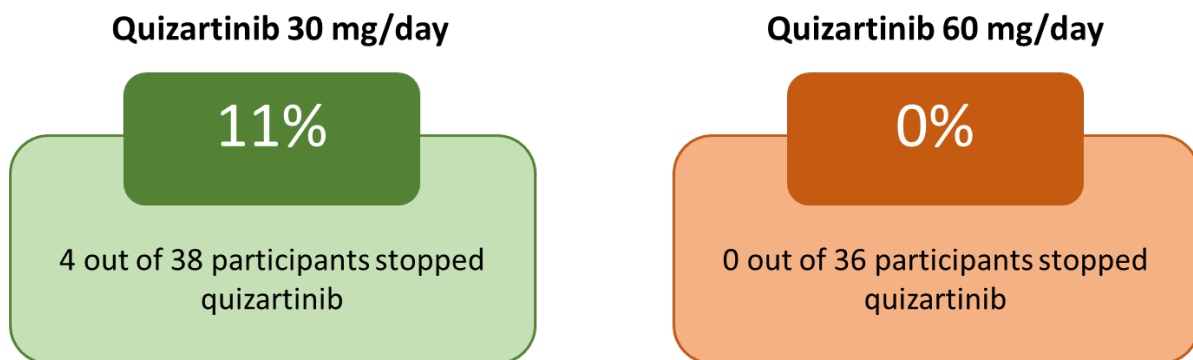
The most common side effects that occurred in at least 10% (10 out of 100) of participants in any group were:





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

### Percentage of participants who stopped quizartinib because of side effects



The side effects that caused participants to stop quizartinib were: abnormal accumulation of fluid around lungs as well as heart, swelling around the heart, diarrhoea, and infection due to low number of platelets.

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


This study helped researchers to learn about the effects and safety of quizartinib in people with relapsed or refractory AML. Based on the results of this study, researchers decided that 60 mg was the maximum dose to be taken forward into 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 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](http://www.clinicaltrials.gov): Use the NCT identifier NCT01565668 in the search field.

 <https://www.clinicaltrialsregister.eu/ctr-search/search>: Use the EudraCT identifier 2011-005408-13 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 2, Randomized, Open Label Study of the Safety and Efficacy of Two Doses of Quizartinib (AC220; ASP 2689) in Subjects with FLT3-ITD Positive Relapsed or Refractory Acute Myeloid Leukemia (AML).

**Sponsor:** Daiichi Sankyo, Inc.

### **Sponsor contact information:**

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

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

**Date of this summary:** 25 March 2021

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