Daiichi-Sankyo

# Clinical Results Summary

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

**Also called:** QuANTUM-R Study

**Protocol number:** AC220-007

**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?

## Increasing the lifespan of people with acute myeloid leukemia

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 to their first treatment (known as refractory AML) or
- responded but their disease came back again within 6 months of receiving their first 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 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. 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 see how effective quizartinib is at treating patients with refractory or relapsed FLT3-ITD positive AML compared to standard chemotherapy.

## Treatments given in this study

**Quizartinib**
(Investigational drug)

An investigational drug being tested for the treatment of AML participants tested positive for FLT3-ITD

**Standard Chemotherapy**
(Approved drugs)

**LoDAC** – low-dose cytarabine (or)
**MEC** - mitoxantrone, etoposide and intermediate-dose cytarabine (or)
**FLAG-IDA** – fludarabine, cytarabine and granulocyte-colony stimulating factor with idarubicin

## Main purpose of this study

The main question the researchers wanted to answer in this study was:

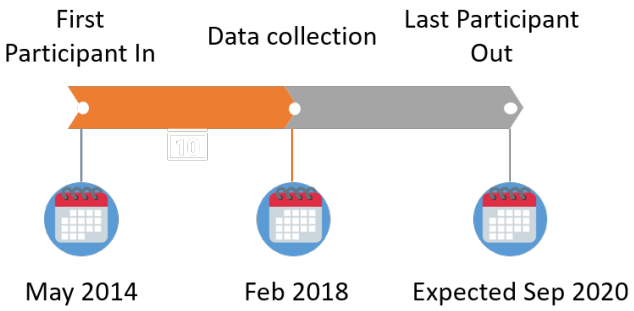
Did participants who took quizartinib live longer than those who took the standard chemotherapy?

Other questions researchers wanted to answer in this study were:

- Did participants who took quizartinib have more time until it was confirmed that the treatment did not benefit them, their disease came back, or they died due to any cause, compared to those who took the standard chemotherapy?
- What medical problems did participants have during the study in the quizartinib group versus the standard chemotherapy group?

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

## How long was this study?

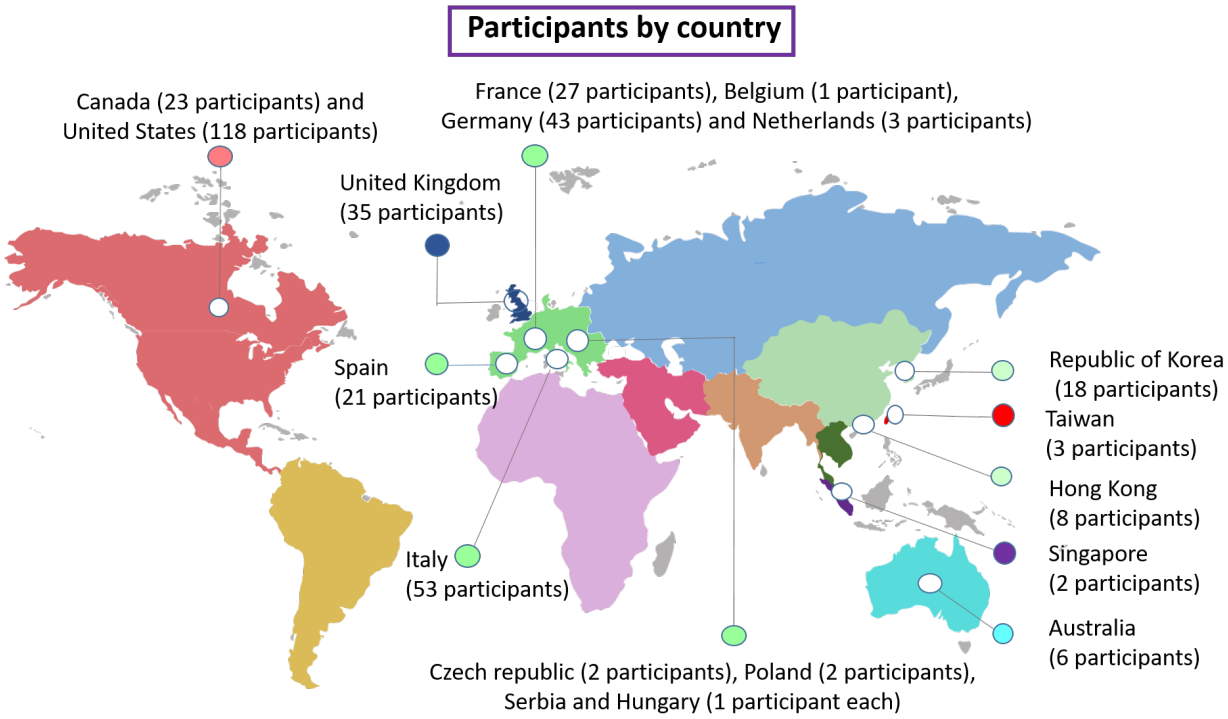



The study was designed in such a way that the participants could continue in it as long as they benefited from the treatment and their AML did not get worse, and they didn't have any serious side effects. A serious side effect could have caused a participant to discontinue their treatment with quizartinib or standard chemotherapy. The first participant was enrolled in the study in May 2014.

The results were collected up to February 2018 for the study report. This summary is based on that report. Some participants are still being followed up and their information is being collected. This is expected to end by September 2020.

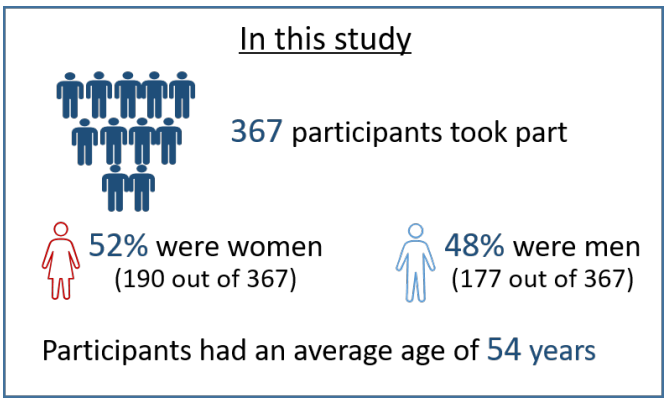
# Who was in this study?

This study included 367 participants from the following countries:



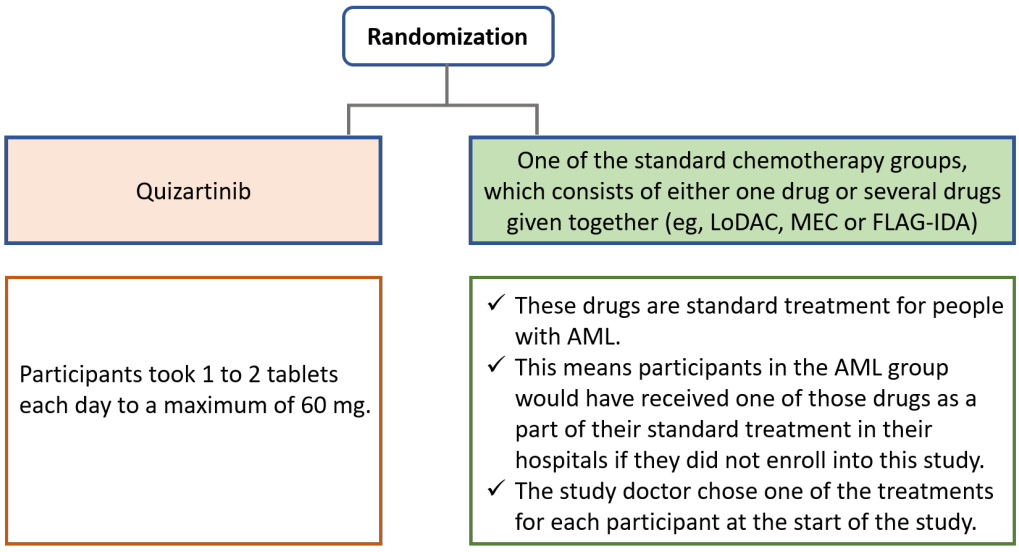
Participants could take part in this study if they:

- were diagnosed with AML or had another type of rare blood cancer that progressed to AML,
- were at least 18 years or 20 years old, depending on which country the participants were based,
- tested positive for the FLT3-ITD mutation,
- were previously treated for AML using standard intensive treatment,
- did not respond to their first AML treatment, or did respond and were free of disease but only for less than 6 months and then their AML came back,
- did not have any major heart problems such as an irregular heart rhythm,
- 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,
- did not have any other diseases or abnormal lab tests that could prevent them from attending study visits and assessments.



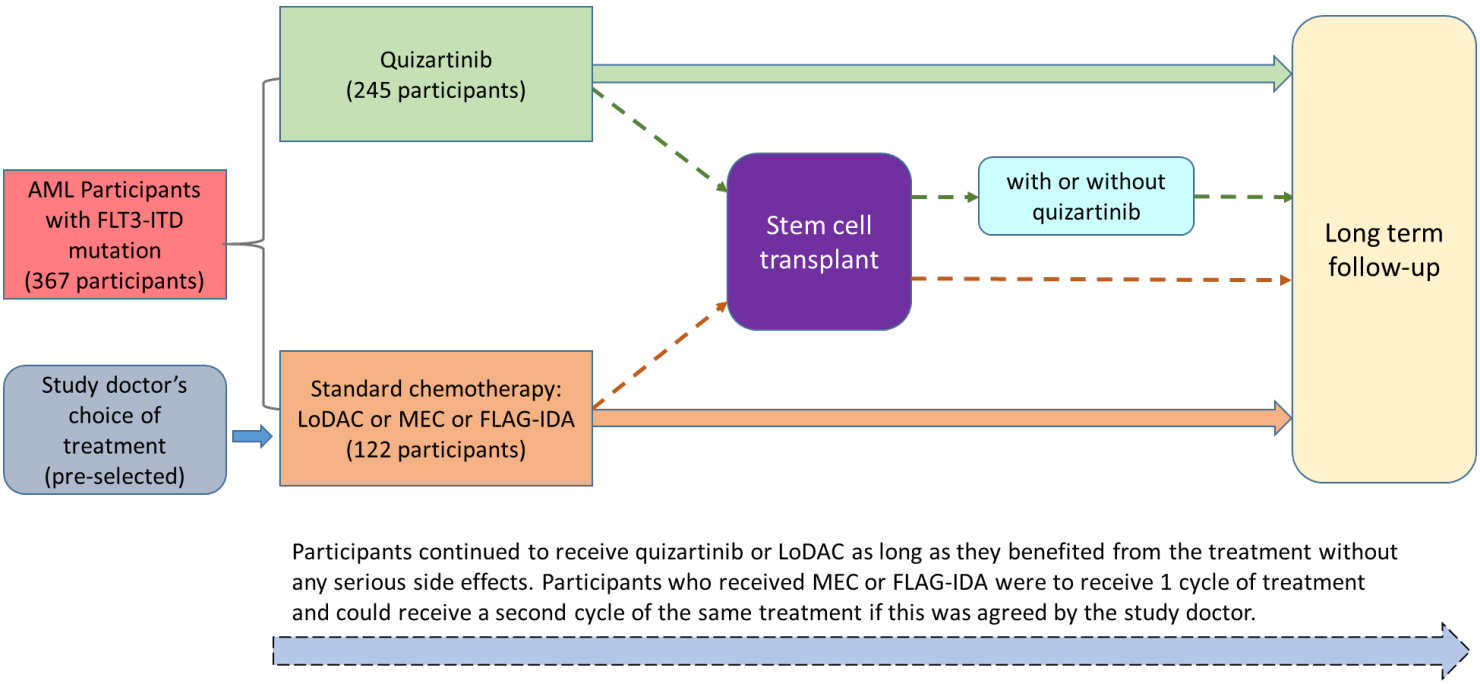

## What happened during this study?

Participants completed a screening period to confirm if they could take part in the study. Researchers used a computer system to assign participants into 2 groups by a process called randomization.



The system was designed to ensure that 2 out of 3 participants received quizartinib and 1 out of 3 participants received one of the standard chemotherapy group treatments.

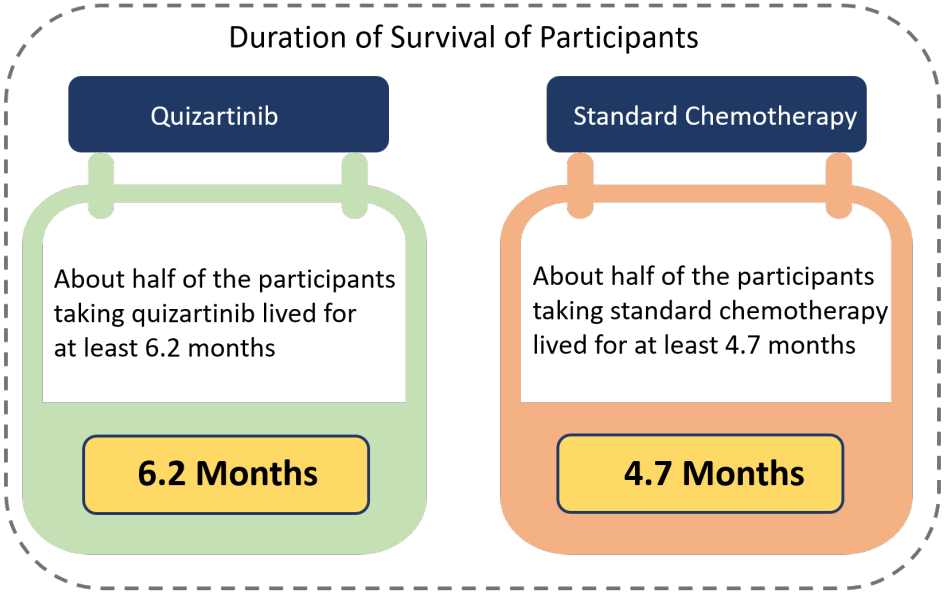
This was an open-label study, meaning the study doctors, the participants and the researchers knew what treatment was given. Participants in both the groups could have a stem cell transplant after receiving treatment and then enter the long term follow-up period. Participants could also enter long term follow-up directly without having had a stem cell transplant. Treatment with quizartinib could be continued after the stem cell transplant for those participants in the quizartinib group. During the long term follow-up, the participants well-being was 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.

Did participants who took quizartinib live longer than those who took the standard chemotherapy?




## What were the other results of this study?

### Did participants who took quizartinib have more time until it was confirmed that the treatment did not benefit them, their disease came back, or they died due to any cause, compared to those who took standard chemotherapy?

Researchers measured the following events for each participant from the time they entered the trial until:

- It was proven that the treatment did not benefit the participant, or
- the disease came back again after responding to the treatment, or
- the participant died due to any cause, whichever happened first.

Participants in both treatment groups had about the same amount of time before any of the above events occurred.

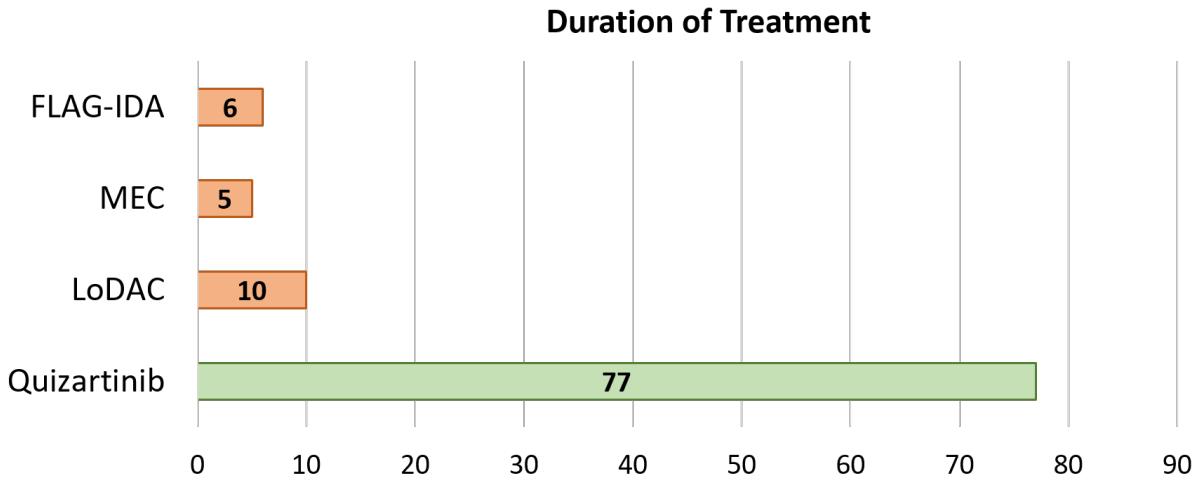
# What medical problems did the study participants have?

Side effects are medical problems (such as feeling tired) 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, lasting problems, birth defects, or require hospitalization. Some participants stopped study treatment because of side effects.

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

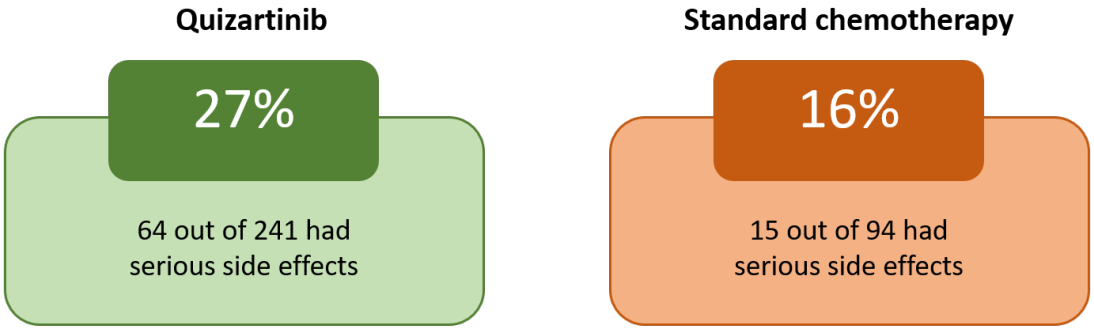
The participants who took quizartinib were in the study longer than the participants who took standard chemotherapy. The figure below shows the median duration for which the participants received either quizartinib or standard chemotherapy (FLAG-IDA, MEC or LoDAC). Median means the midpoint value for a group. For example, in the group of the participants who were treated with quizartinib, the duration of the treatment for half of them was less than 77 days and for the other half  it was more.



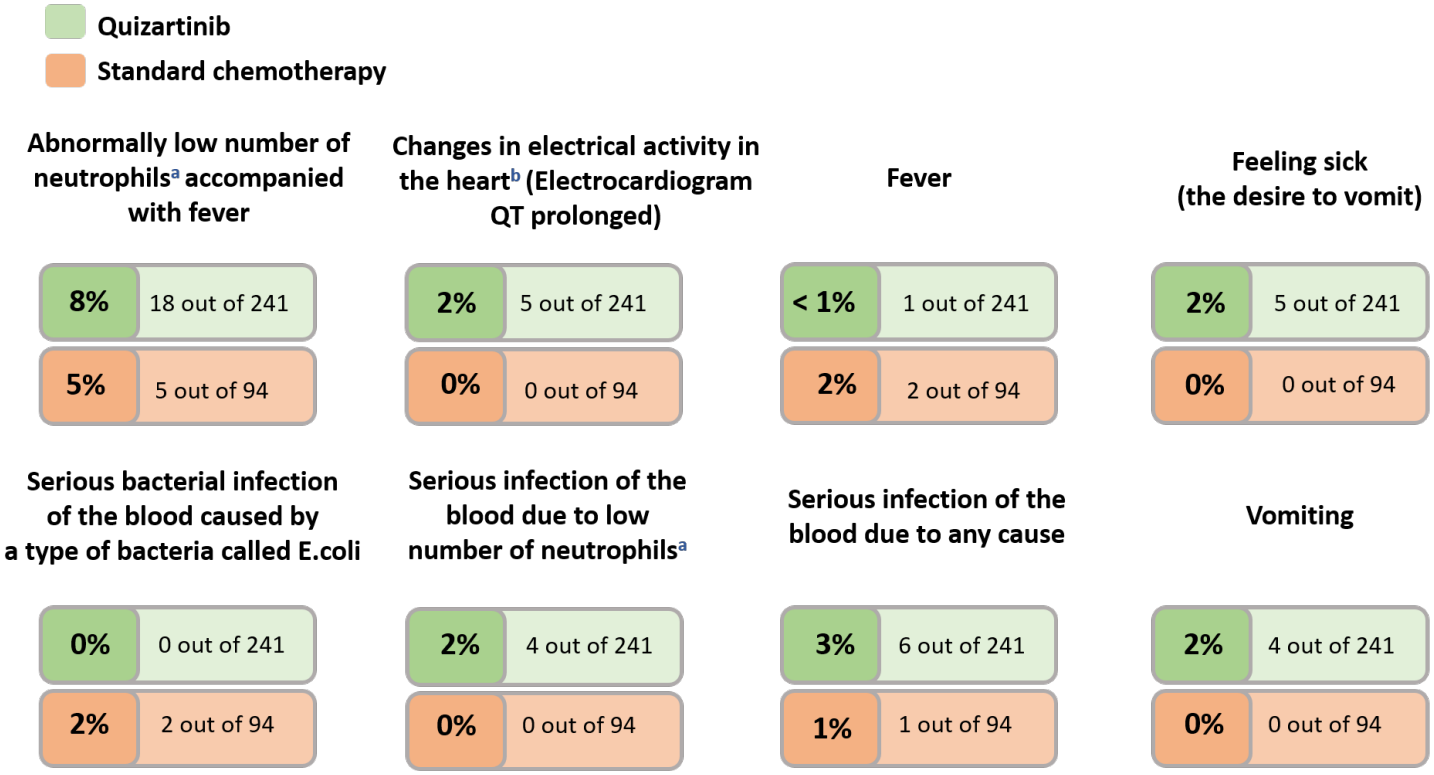

## How many participants had serious side effects?

In this study, side effects were monitored for 241 participants who took quizartinib and 94 participants who took standard chemotherapy.

**Percentage of participants who had serious side effects**

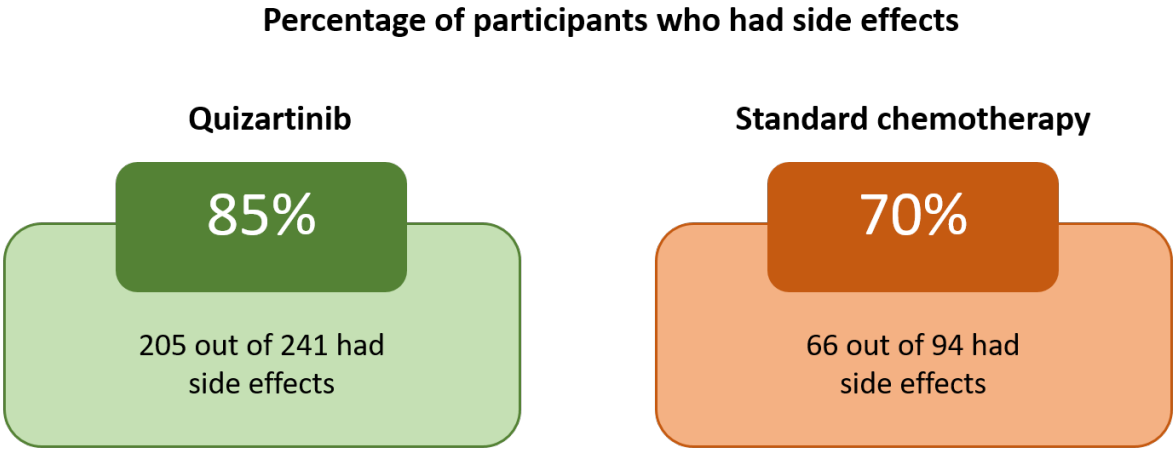



The most common serious side effects that occurred in at least 2% (2 out of 100) of participants in any group are reported below:

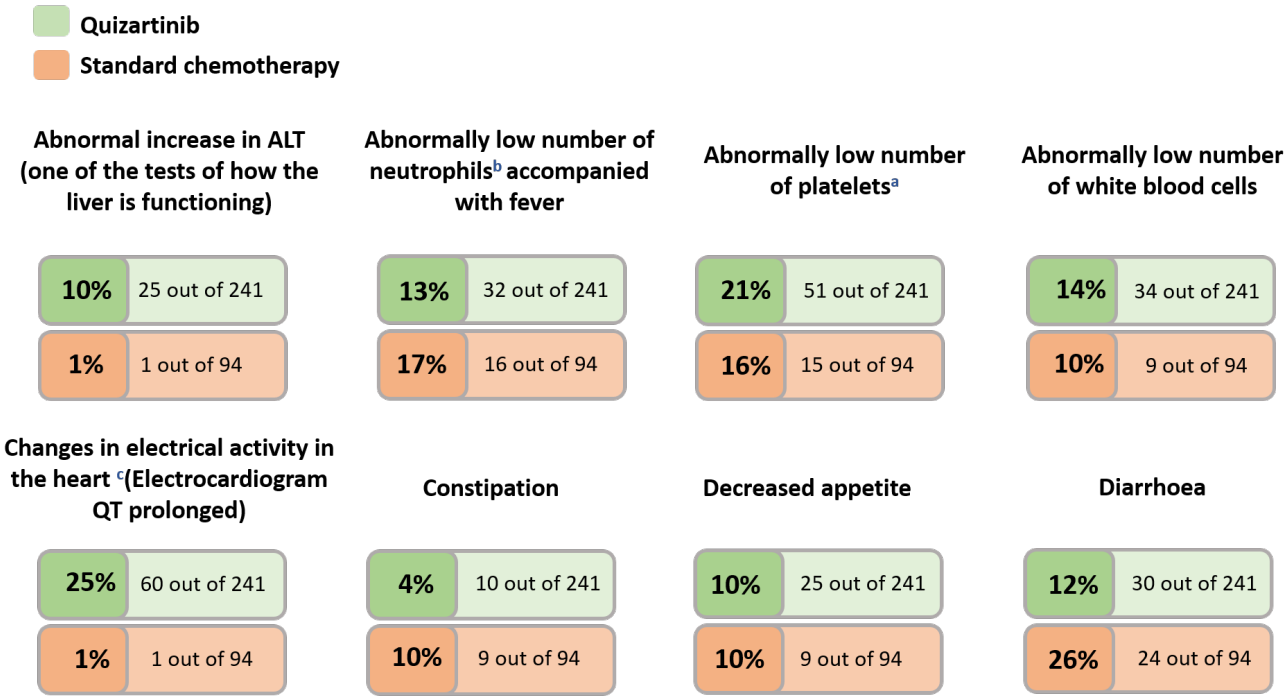



a: A type of white blood cell that fights bacteria
b: Detected using an ECG of the heart

## How many participants had side effects?




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



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

| | |
|---|---|
| 33% | 80 out of 241 |
| 34% | 32 out of 94 |

**Fever**

| | |
|---|---|
| 8% | 19 out of 241 |
| 16% | 15 out of 94 |

**Low haemoglobin levels in blood**

| | |
|---|---|
| 25% | 60 out of 241 |
| 21% | 20 out of 94 |

**Low number of neutrophils[b]**

| | |
|---|---|
| 12% | 28 out of 241 |
| 11% | 10 out of 94 |

**Low number of platelets[a]**

| | |
|---|---|
| 11% | 27 out of 241 |
| 10% | 9 out of 94 |

**Low number of white blood cells**

| | |
|---|---|
| 12% | 30 out of 241 |
| 13% | 12 out of 94 |

**Low potassium levels in the blood**

| | |
|---|---|
| 10% | 23 out of 241 |
| 9% | 8 out of 94 |

**Sore and inflamed mouth**

| | |
|---|---|
| 5% | 13 out of 241 |
| 17% | 16 out of 94 |

**Swelling of the lower legs or hands**

| | |
|---|---|
| 5% | 12 out of 241 |
| 11% | 10 out of 94 |

**Vomiting**

| | |
|---|---|
| 20% | 48 out of 241 |
| 15% | 14 out of 94 |

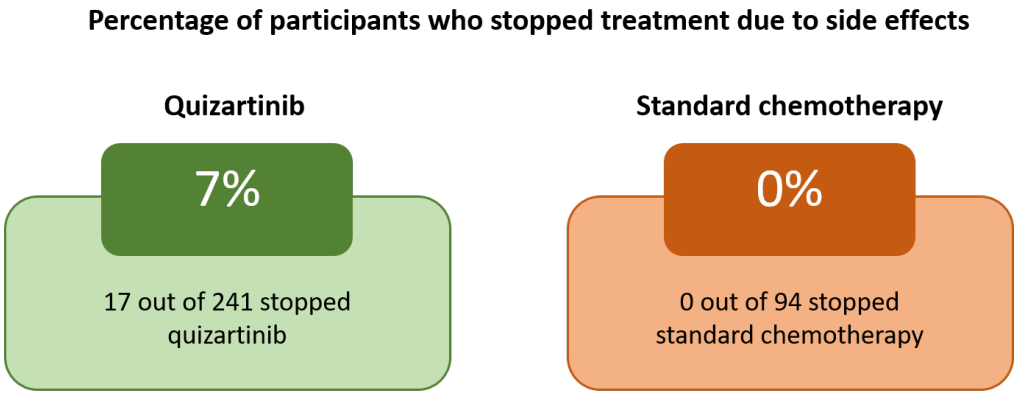
**Weakness**

| | |
|---|---|
| 16% | 39 out of 241 |
| 15% | 14 out of 94 |

a. A type of blood cell that helps in preventing/stopping bleeding.
b. A type of white blood cell that fights bacteria.
c. Detected using an ECG of the heart.

In total, there were 13 deaths reported in this study possibly related to study drug, 9 on quizartinib and 4 on standard chemotherapy. Overall, the most common reason was infection.

## How many participants had to stop treatment due to side effects?




Changes in electrical activity in the heart (Electrocardiogram QT prolonged) was the most common side effect for participants to stop study treatment. It happened in 2 participants.

# How was this study useful for patients and researchers?

This study helped researchers learn about how quizartinib is able to increase the lifespan of participants since they started treatment compared to participants who took standard chemotherapy.

Findings from this study may be used to seek approval to use study treatment in patients with AML who have tested positive for FLT3-ITD mutation.

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 NCT02039726 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search: Use the EudraCT identifier 2013-004890-28 in the search field.
- https://www.nccn.org/patients/guidelines/content/PDF/aml-patient.pdf: The National Comprehensive Cancer Network® (NCCN) guidelines for patients: acute myeloid leukemia, 2020.

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 3 Open-label Randomized Study of Quizartinib Monotherapy Versus Salvage Chemotherapy in Subjects With FLT3-ITD Positive Acute Myeloid Leukemia (AML) Refractory to or Relapsed After First-line Treatment With or Without Hematopoietic Stem Cell Transplantation (HSCT) Consolidation

**Sponsor:** Daiichi Sankyo, Inc.

**Sponsor contact information:**
CTRInfo@dsi.com, Tel: +1 (908) 992-6640 for any queries related to the summary.

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

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