Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the effects of quizartinib given with standard chemotherapy in people with a type of blood cancer called FLT3-ITD positive acute myeloid leukemia

Also called: QuANTUM-First

Protocol number: AC220-A-U302

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 for people affected with a type of blood cancer called FLT3-ITD positive 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?

Researchers were looking for a better way to treat people with acute myeloid leukemia, or AML.

Acute Myeloid Leukemia

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, circulate in the blood, and go to different parts of the body.

Treatment for AML is usually given in 3 stages:

- **Induction stage** – to kill cancer cells and allow normal cells to grow in the bone marrow and blood.
- **Consolidation stage** – to lower the risk of the cancer coming back. Treatment options include chemotherapy, or in certain cases a stem cell transplant.
- **Maintenance stage** – to lower the risk of the cancer coming back. Treatment is given over a longer period of time and often at lower doses or using targeted agents depending on your leukemia.

Chemotherapy uses medicines to kill cancer cells. In this study, the patients were given chemotherapy through a drip into a vein for AML. 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.

People with AML can have certain gene changes (or mutations). A gene contains information to make proteins in the body, these proteins help in different functions in the body. A change in gene affects the functions in the body. People with FLT3-ITD positive AML have a change 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.

In this study, researchers wanted to learn more about the effect of quizartinib given with standard chemotherapy in people newly diagnosed with FLT3-ITD positive AML.

Treatments given in this study

The treatments given in this study were:

Quizartinib
(40 mg, Tablet)
An investigational drug being tested for the treatment of FLT3-ITD positive AML. Quizartinib is designed to work against AML cells with the FLT3-ITD mutation

Placebo
(Tablet)
A placebo looks like the study treatment and is given in the same way, but does not have any medicine in it. Researchers sometimes use a placebo to understand if the changes seen were due to the study treatment or if they happened by chance

Standard Chemotherapy
(As drip in the vein)
Induction therapy
Cytarabine
Daunorubicin OR Idarubicin
Consolidation therapy
Cytarabine only

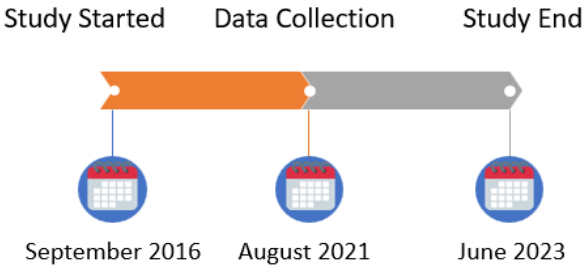
Main purpose of this study

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

How long did the participants* live after the start of the treatment with quizartinib until they died due to any cause compared to placebo?

*Participants were newly diagnosed with FLT3-ITD positive AML

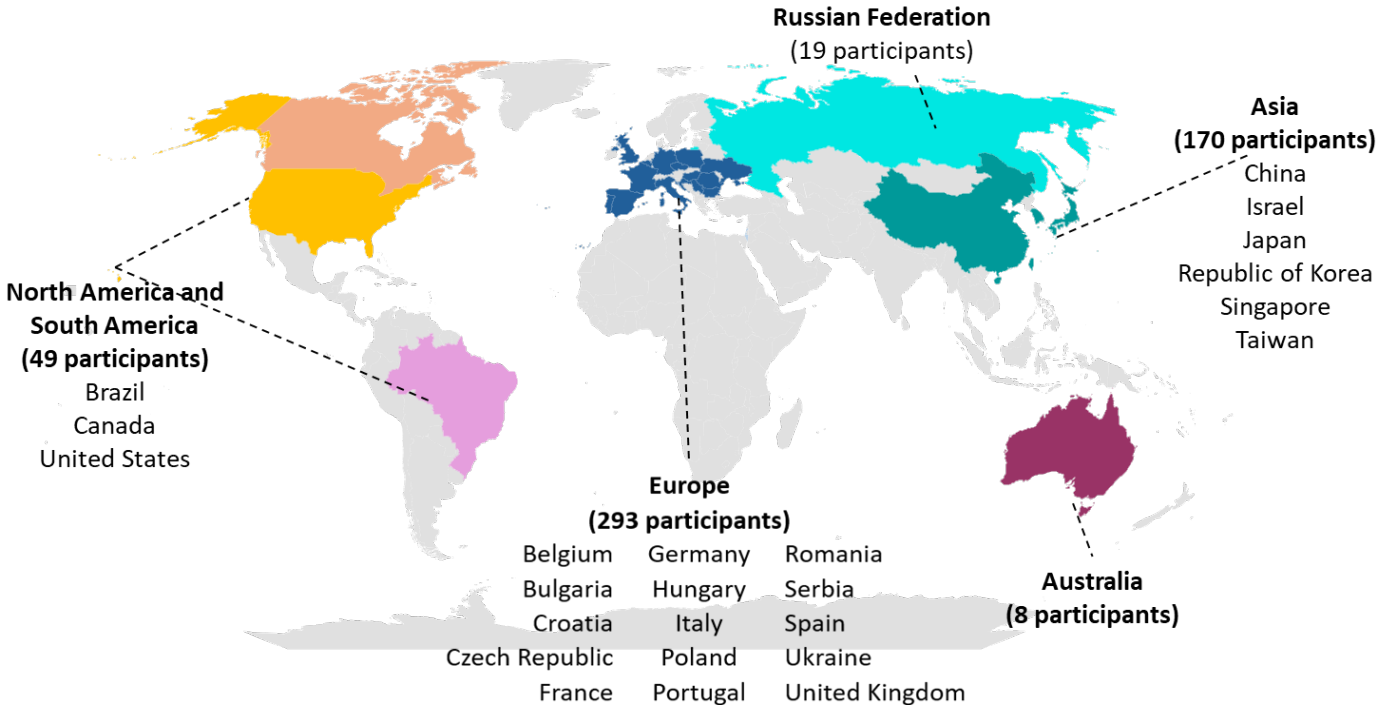
How long was this study?



The study was designed such that participants could continue in it as long as their cancer did not get worse, they did not have serious side effects, or met certain criteria to stop study treatment. The study started in September 2016 and ended in June 2023.

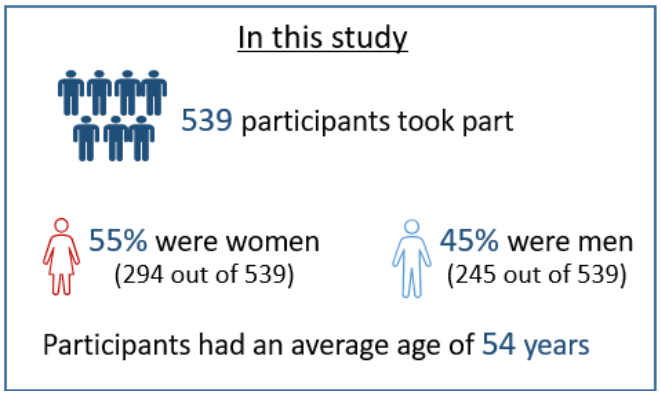
Who was in this study?

This study included 539 participants from the following regions:



Participants could take part in this study if they:

- were 18 to 75 years old,
- had a certain disease of the bone marrow or blood,
- tested positive for FLT3-ITD mutation,
- had adequately functioning heart, liver and kidneys,
- were either fully active or could move and were able to carry out work of a light nature or just self-care.



What happened during this study?

This was a Phase 3 study that compared quizartinib with placebo, both given with standard chemotherapy.

In Phase 3 studies, the study treatment is given to a large number of participants with the disease condition to learn more about the effects of the study treatment and its safety.

Researchers assigned participants to treatment groups by chance using a computer system. This process is called randomization. It means that each participant could be assigned to any group, and it helps to make sure the groups are distributed fairly.

This study was "double blind". This means that neither participants nor the researchers knew who was given which treatment. Studies are sometimes done this way to make sure that study results are not biased by this information.

The study consisted of 4 stages: induction stage, consolidation stage, continuation stage, and long-term follow-up stage.

Induction stage, participants received quizartinib and placebo tablets with standard induction chemotherapy (cytarabine and either daunorubicin or idarubicin given as drips) for 1 to 2 cycles (1 cycle was for 28 days). The participants who responded with 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: 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 transfusion.

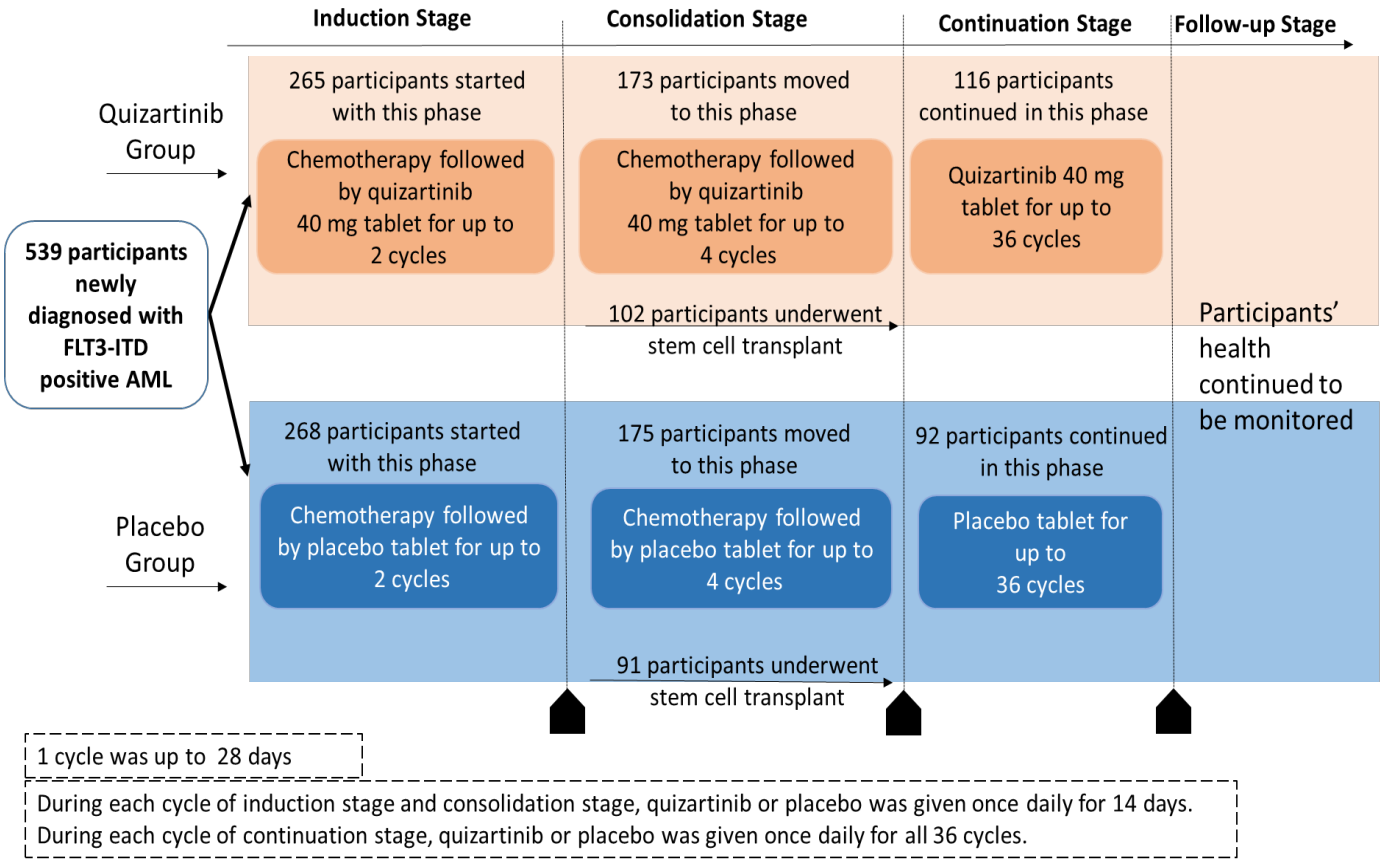
CRi: means less than 5% of cells in the participant's bone marrow were cancer cells, with incomplete recovery of neutrophils, with or without complete recovery of platelets. The participants may or may not have needed a blood or platelet transfusion.

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, participants received quizartinib and placebo tablets with standard consolidation chemotherapy (cytarabine only given as drips) for up to 4 cycles (1 cycle was for 28 days). Participants continued to the consolidation phase only if they achieved CR or CRi at the end of induction stage. The participants who achieved CR or CRi after induction stage or later could go on to receive a stem cell transplant.

Continuation stage, participants continued receiving quizartinib or placebo tablets for up to 36 cycles (1 cycle was for 28 days).

Long-term follow-up stage, all the participants who completed 36 cycles of study treatment in the continuation phase or stopped study treatment during any stage were followed up to monitor their overall health.

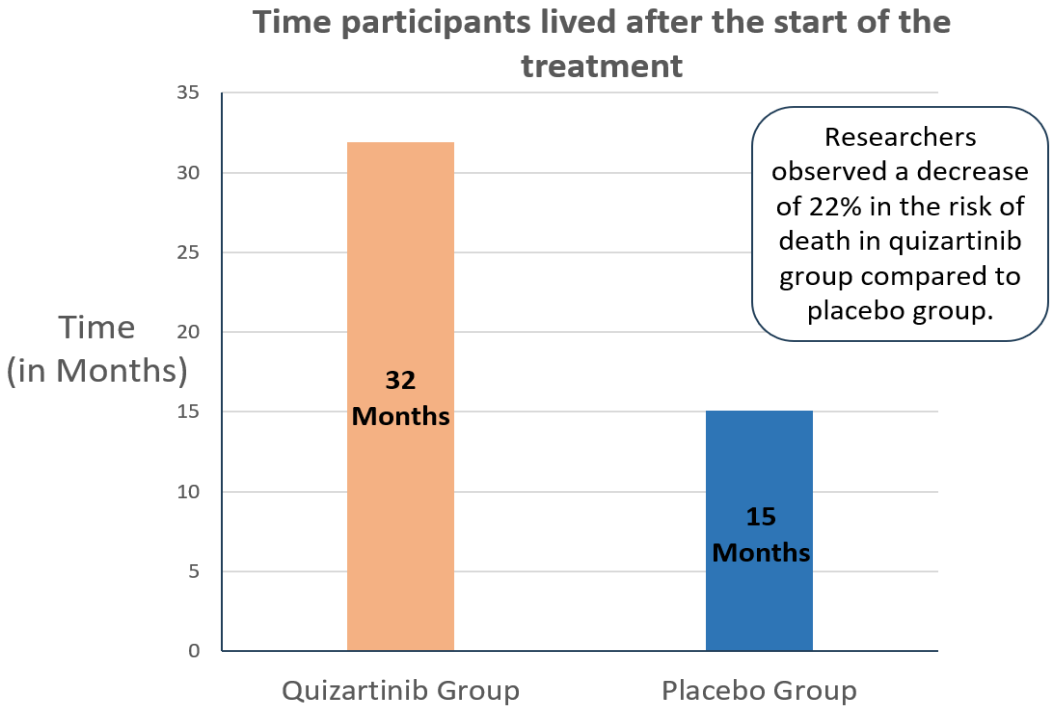


What were the key results of this study?

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 long did the participants live after the start of the treatment with quizartinib compared to placebo until they died for any reason?

To answer this question, researchers measured the time from starting the treatment until the participants died for any reason (disease or non-disease related reasons).



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 (investigator) thought could be related to the treatments in the study. This section provides a summary of side effects related to the study treatment. The website listed at the end of this summary has more information about the medical problems that happened in this 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 stop study treatment because of side effects.

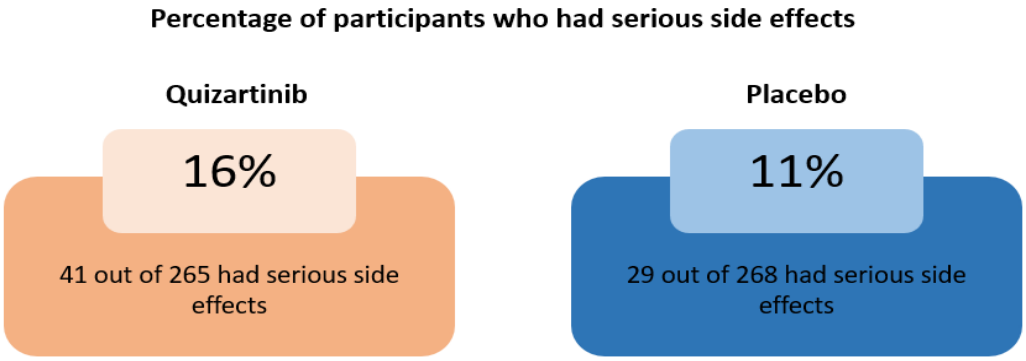
Side effects other than those related to study treatment are not reported here. For more information on medical problems, please visit the websites listed at the end of this summary. This section includes results for all the participants who received at least one dose of study treatment along with standard chemotherapy.

In this study, 533 out of the 539 participants were monitored for side effects as 6 participants did not receive any study treatment.

How many participants had serious side effects?

In this study, side effects were monitored for 265 participants in quizartinib group and for 268 participants in placebo group.

41 out of 265 (16%) participants in quizartinib group and 29 out of 268 (11%) participants in placebo group had serious side effects as shown in the table below.



Quizartinib (out of 265 participants) Percentage (number of participants)	Serious side effects	Placebo (out of 268 participants) Percentage (number of participants)
3% (7)	Abnormally low number of neutrophils* accompanied with fever	2% (4)
2% (4)	Lung infection/Worsening of chest infection	1% (2)
1% (3)	Decrease in production of blood cells in bone marrow	0%
1% (3)	Low neutrophil count	0%
0%	Body's extreme response to an infection	1% (3)

*Neutrophils are a type of white blood cell that help fight infections

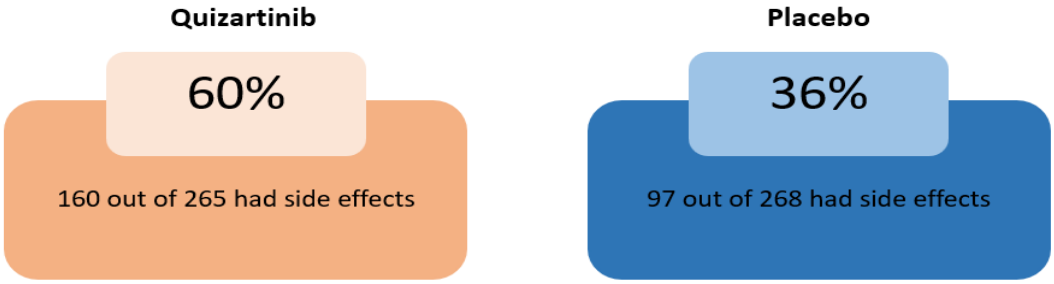
4 participants in quizartinib group died during this study. The causes of death were a fungal infection called mucormycosis, a stroke, shock due to very low blood pressure caused by infection and a clot in a blood vessel in the lungs.

4 participants in placebo group died during this study. The most common causes of death were lung damage, fungal infection called mycosis, bleeding of the lungs and infection of the lungs.

How many participants had side effects?

61% (161 out of 265) participants in quizartinib group reported side effects and
36% (97 out of 268) participants in placebo group reported side effects. The most common side effects that happened in at least 5% of participants in either treatment group are shown below.

Percentage of participants who had side effects

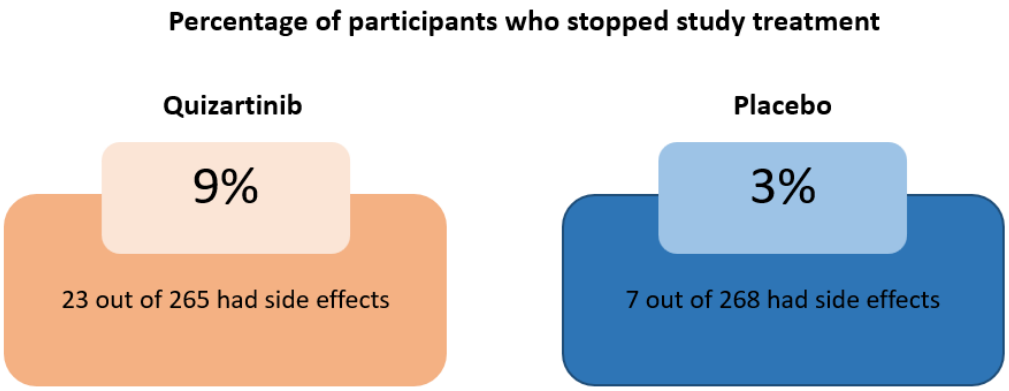


Quizartinib (out of 265 participants) Percentage (number of participants)	Most common side effects	Placebo (out of 268 participants) Percentage (number of participants)
17% (46)	Low neutrophil count	4% (10)
12% (31)	Changes in electrical activity in the heart[+] (Electrocardiogram QT prolonged)	3% (8)
9% (24)	Feeling sick (the desire to vomit)	5% (12)
9% (23)	Abnormally low number of neutrophils* accompanied by fever	8% (20)
8% (21)	Decreased neutrophil count	2% (5)
7% (18)	Diarrhea	7% (19)
7% (18)	Low blood platelet count	5% (13)
6% (15)	Low number of red blood cells	3% (9)
6% (15)	Increase in blood levels of an enzyme called alanine aminotransferase that may indicate liver damage	3% (7)
5% (14)	Fever	4% (10)

[+]Detected using an ECG of the heart
*Neutrophils are a type of white blood cell that help fight infections

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

9% (23 out of 265) participants in quizartinib group stopped study treatment early because of side effects.
3% (7 out of 268) participants in placebo group stopped treatment early because of side effects.



How was this study useful for patients and researchers?

This study helped researchers understand how long participants with newly diagnosed FLT3-ITD positive AML lived after starting treatment with quizartinib compared to placebo, both given in combination with standard chemotherapy.

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Findings from this study may be used in other studies to learn whether patients with FLT3-ITD positive AML are helped by this treatment. Other studies for quizartinib are ongoing and the sponsor plans to conduct (any) more studies in the future.

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 NCT02668653 in the search field.
- www.clinicaltrialsregister.eu/ctr-search/search: Use the EudraCT identifier 2015-004856-24 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 3, Double-blind, Placebo-controlled Study of Quizartinib Administered in Combination with Induction and Consolidation Chemotherapy, and Administered as Continuation Therapy in Subjects 18 to 75 Years Old with Newly Diagnosed *FLT3*-ITD (+) Acute Myeloid Leukemia (QuANTUM-First)

Sponsor: Daiichi Sankyo, Inc.

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