Clinical Results Summary

A clinical study to learn about the plasma levels of quizartinib in healthy people compared to people with liver disease

Protocol number: AC220-016

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 and knowledge for people affected with 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)

Quizartinib is an investigational drug being tested for the treatment of acute myeloid leukemia, or AML.

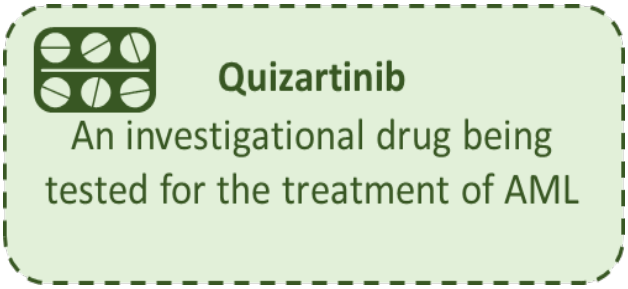
AML is a cancer of the blood and bone marrow. The bone marrow is found in the center of most bones, where new healthy blood cells are made. AML starts in the bone marrow and prevents it from making normal blood cells. The abnormal (cancer) cells build up in the bone marrow, so there are fewer healthy blood cells. These cancerous cells can also enter the blood stream and circulate in the blood, and go to different parts of the body.

Before a new drug can be given to patients, the researchers developing it perform many research studies to show that the drug is safe and effective. The first step in studying a new drug is to test it in healthy people. This means people without any serious health problems. This study involved healthy participants.

In the studies done so far, researchers learned that the liver plays an important role in removing quizartinib from the body. Therefore in this study, researchers wanted to compare the plasma* levels of quizartinib and its breakdown product AC886 in people with liver disease with the plasma levels in healthy people. This will enable researchers to decide what dose of quizartinib should be given to people with liver disease.

* Plasma is the fluid part of the blood. It contains different components of the blood that are necessary for life and health such as hormones, proteins, etc.

Treatment given in this study



Main purpose of this study

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

What is the effect of mild to moderate liver disease on the plasma levels of quizartinib and its breakdown product AC886?

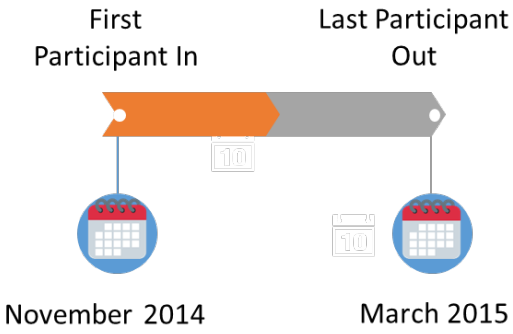
Other purpose of this study

Researchers also wanted to answer the following question:

- What side effects could the participants develop during the study?

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

How long was this study?

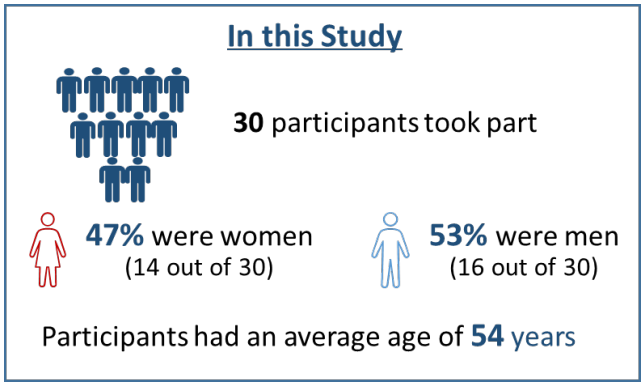


An individual participant could have been in this study for 30 days.

The study started in November 2014 and was completed as planned in March 2015. A study report was created. This summary is based on that report.

Who was in this study?

This study included 30 participants from United States.



Participants could take part in this study if they:

- were aged 18 to 70 years of age
- had previously been diagnosed with liver disease, and were assessed as having mild or moderate liver disease as measured by a scoring system*
  OR
  were healthy, as assessed by the study doctor
- were willing to eat high-potassium foods, such as bananas, at least 24 hours before taking quizartinib on Day 1 of the study
- used effective birth control methods during the study or were unable to have children.

* The Child-Pugh scoring system, or CPS, was used to find out whether participants had mild or moderate liver disease by using 5 clinical measures (symptoms & signs). A score of 1, 2, or 3 was given to each measure, with 3 being the most severe. The scores were added for all 5 measures. Out of a maximum score of 15, only participants with scores of 5 to 6 (mild liver disease), or 7 to 9 (moderate liver disease) were included 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 the body, and if there are any side effects.

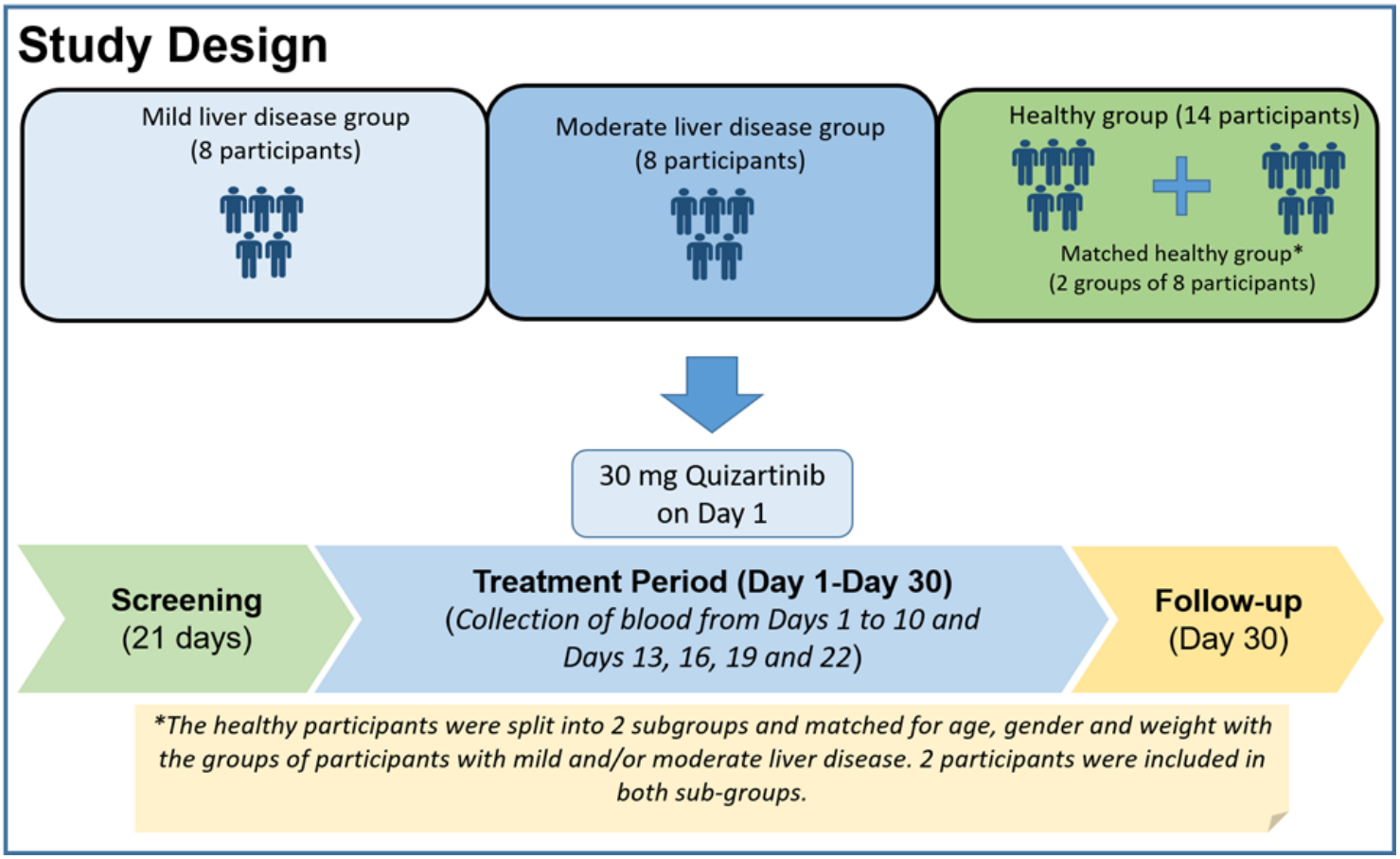
This study was “open label”. This means that both the researchers and the participants knew which treatment was given to which participants.

Participants were screened to find out if they could take part in the study. All participants received 30 mg quizartinib tablets on only one day in the study (Day 1), on an empty stomach. Participants continued fasting for 4 hours after taking the quizartinib tablets.

There were 3 groups of participants:

- 8 participants with mild liver disease,
- 8 participants with moderate liver disease, and
- 14 healthy participants

The healthy participants were split into 2 subgroups and matched for age, gender and weight with the groups of participants with mild and/or moderate liver disease. These 2 subgroups of healthy participants served as control groups for the 2 groups of participants with mild or moderate liver disease. Within these control groups, 2 participants had appropriate age, gender and weight measurements which allowed them to serve as controls for both groups of participants with mild and/or moderate liver disease. Therefore although there were only 14 healthy participants in the study, this meant there were 8 participants in each of the matched healthy contol groups.



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 was the effect of mild to moderate liver disease on the plasma levels of quizartinib and its breakdown product AC886?

The total plasma levels of quizartinib and AC886 measured over time were similar in participants with mild or moderate liver disease, when compared with levels in matched healthy participants.

This means that liver impairment disease did not have much effect on the total plasma levels of quizartinib and AC886.

	(8 participants) Mild Liver Problems	(8 participants) Matched Healthy Participants	(8 participants) Moderate Liver Problems	(8 participants) Matched Healthy Participants
The **total level** of **quizartinib** in plasma (ng·hr/ml)	9462	7304	7043	6132
The **total level** of **AC886** in plasma (ng·hr/ml)	3256	2716	1972	3304

How was this measured?

Researchers took blood samples from participants at defined time points and calculated the total levels of quizartinib and AC886 in participants' plasma over time, in ng·h/ mL*.

*This means the total levels of quizartinib and AC886 in nanograms (one thousand-millionth of a gram) found in each milliliter of plasma over time.

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 researchers thought could be related to the treatments in the study.. This section provides a summary of side effects related to quizartinib.

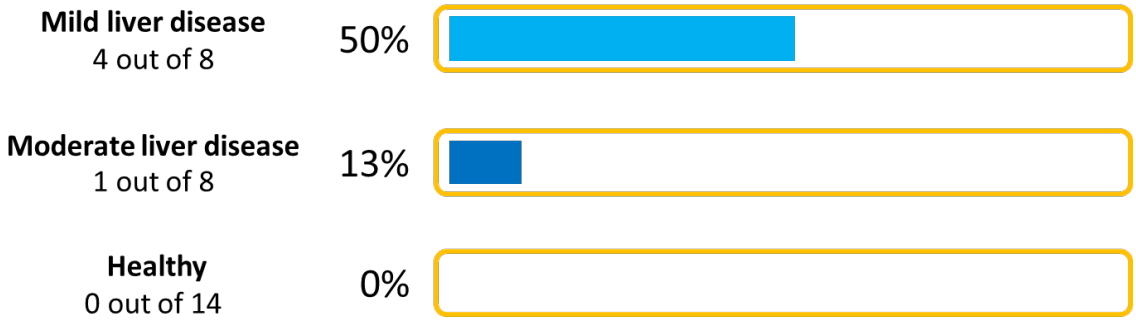
Side effects are considered serious if they cause death, are life-threatening, cause disability, cause lasting problems, cause birth defects, or require hospitalization. Sometimes participants stop taking study treatment because of side effects.

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.

There were no deaths or serious side effects reported during the study that were related to quizartinib. None of the participants in the study stopped quizartinib early because of side effects.

How many participants had side effects?

The side effects experienced by participants in any group are reported below:



Side Effects	Mild Liver * Disease (8 participants)	Moderate Liver Disease (8 participants)	Healthy Participants (14 participants)
Altered taste	13% (1)	0	0
Constipation	13% (1)	0	0
Cough	0	13% (1)	0
Diarrhea	13% (1)	0	0
Headache	13% (1)	0	0
Stomach acid flows back from the stomach to the food pipe	13% (1)	0	0

* One participant with mild liver disease had 2 different side effects.

How was this study useful for patients and researchers?

This study helped researchers to compare the plasma levels of quizartinib and AC886 in healthy people from people with liver disease.

Findings from this study may be used in other studies. Other studies for 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?

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, Open-label, Single-dose, Parallel-group Study to Evaluate the Pharmacokinetics of Quizartinib and its Active Metabolite, AC886, in Subjects with Mild or Moderate Hepatic Impairment Compared to Healthy Subjects

Sponsor: Daiichi Sankyo, Inc.

Sponsor contact information:

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