

Clinical Results Summary

A clinical study to understand the effects of ketoconazole and fluconazole on the plasma levels of quizartinib in healthy participants

Protocol number: AC220-015

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 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?

Quizartinib is an investigational drug that is being tested to treat people with a type of blood cancer called acute myeloid leukemia, or AML. AML is a cancer of the blood and the bone marrow.

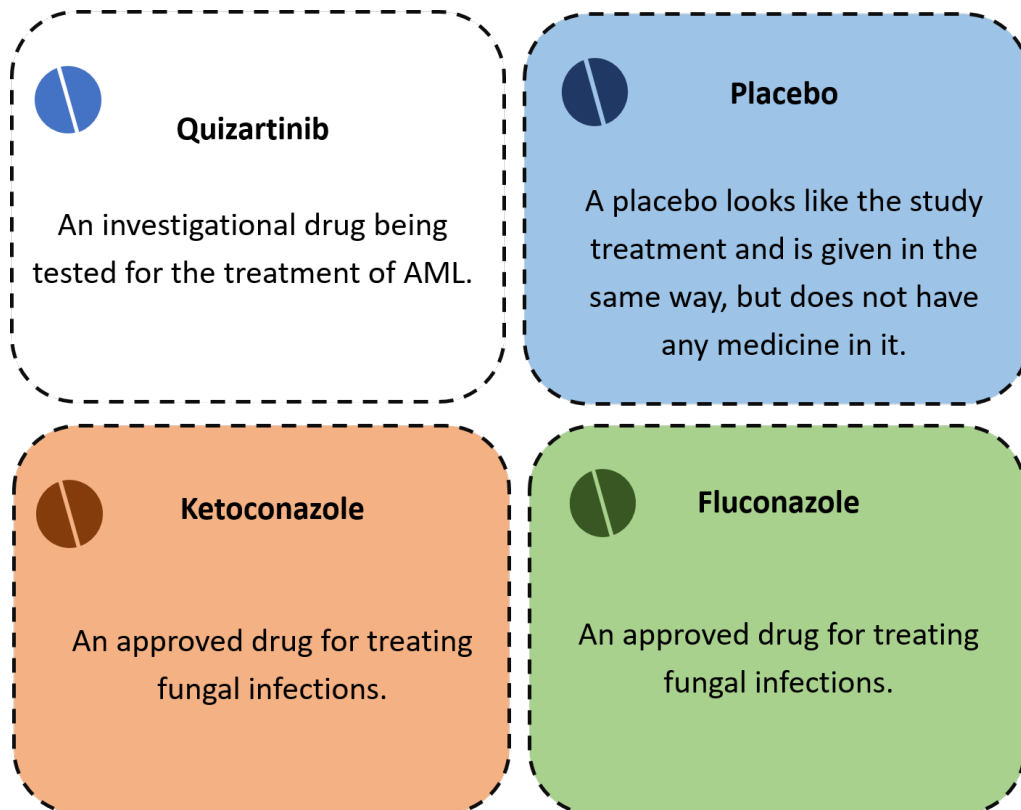
Ketoconazole and fluconazole are drugs already available in the market for treating fungal infections. Both ketoconazole and fluconazole block a protein in the liver called CYP3A4 that breaks down quizartinib in the body. Ketoconazole is a strong inhibitor of CYP3A4 and fluconazole is a moderate inhibitor of CYP3A4. Taking either ketoconazole or fluconazole with quizartinib may slow down the breakdown of quizartinib in the body. If quizartinib is not broken down, it may accumulate in the body and cause harmful effects. AC886 is a breakdown product of quizartinib. It can be formed as a result of quizartinib being broken down by CYP3A4. AC886 has similar effects in the body to quizartinib. Once formed from quizartinib, AC886 can also be further broken down by CYP3A4.

In this study, researchers wanted to understand the effects of ketoconazole and fluconazole on the plasma* levels of quizartinib and its breakdown product AC886 in healthy participants.

** 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.*


Treatments given in this study

The treatments given in this study were:



Main purpose of this study

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

 What is the effect of ketoconazole and fluconazole on the plasma levels of quizartinib and its breakdown product AC886 in healthy participants?

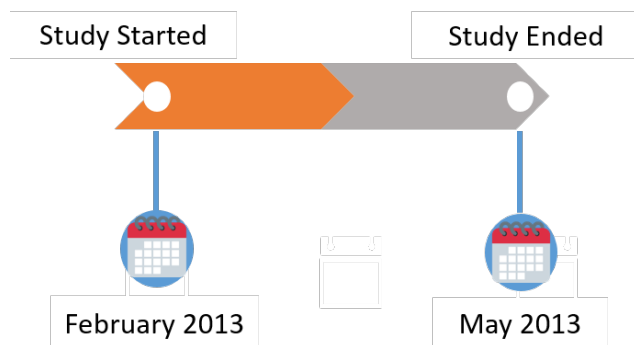
Other purpose of this study

Researchers also wanted to answer the following questions:

- 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?



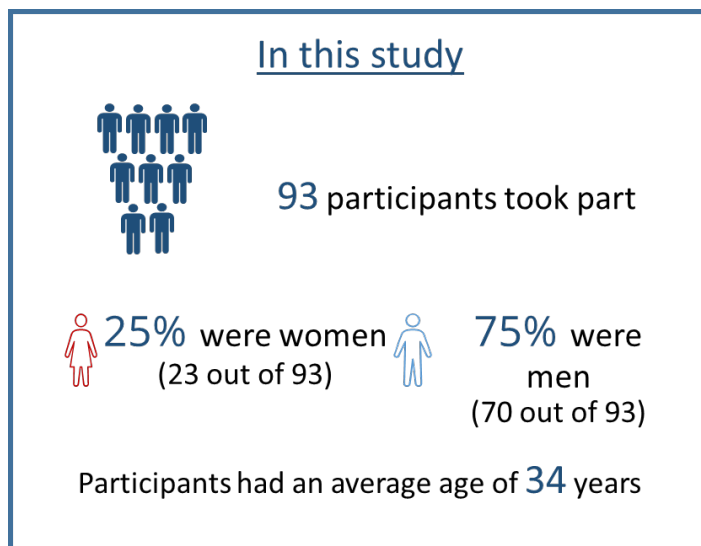
An individual participant could have been in this study for about 2 months.

The study was completed as planned and a study report was created. This summary is based on that report.

Who was in this study?

This study included 93 participants from the United States. Healthy men and women could take part in this study if they:

- were 18 to 55 years of age,
- were of average body size and weight,
- had normal healthy kidneys and liver as measured by different blood tests,
- were using effective birth control methods during the study or were unable to have children,
- were willing to eat high-potassium foods, such as bananas, for at least 24 hours before taking quizartinib,
- were able to communicate in English, and
- were able to follow the study requirements.



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 other drugs such as ketoconazole or fluconazole change quizartinib plasma levels.

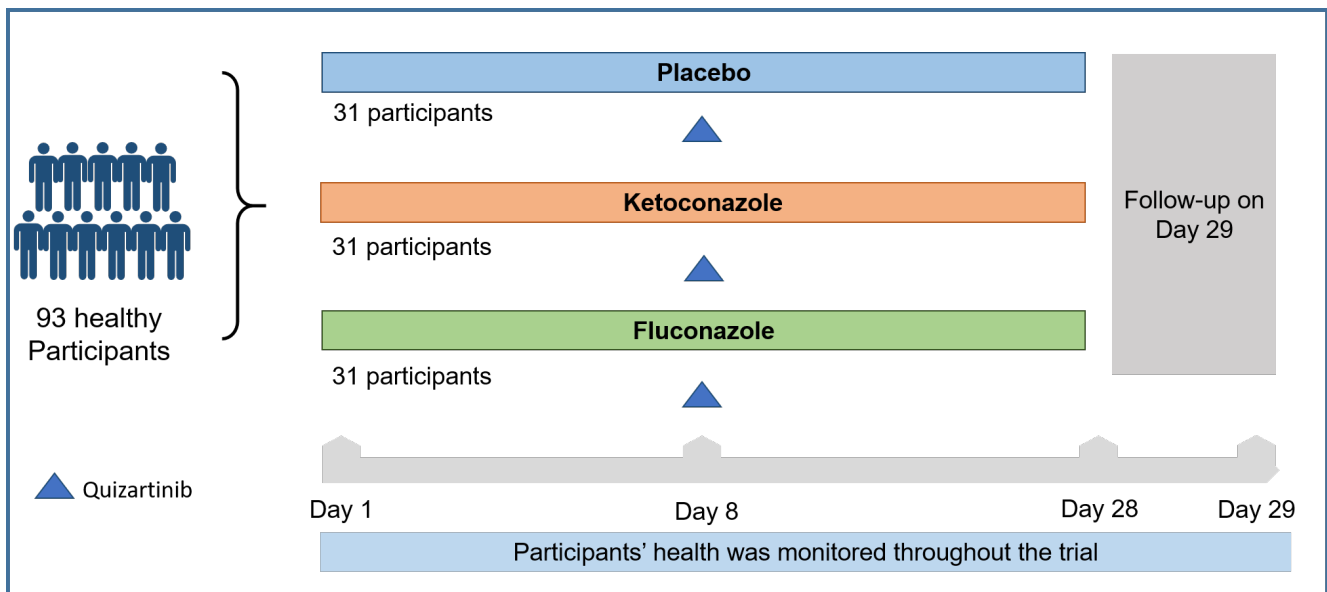
This study was “open label”. This means that both the researchers and the participants knew which treatment was given to which participants.

Participants were randomly assigned to 1 of the 3 treatment groups using a computer system. This process is called randomization. It means that each participant could be assigned to any treatment group to make sure the groups are distributed fairly.

Participants were assigned to one of the following treatment groups:

- Ketoconazole 200 milligrams (mg) twice daily, taken by mouth.
- Fluconazole 200 mg twice daily, taken by mouth.
- Placebo twice daily, taken by mouth.

Participants took placebo, ketoconazole, or fluconazole twice daily from Day 1 to Day 28. Participants in all 3 treatment groups also took a single 30 mg dose of quizartinib only on Day 8.



What were the key results of this study?

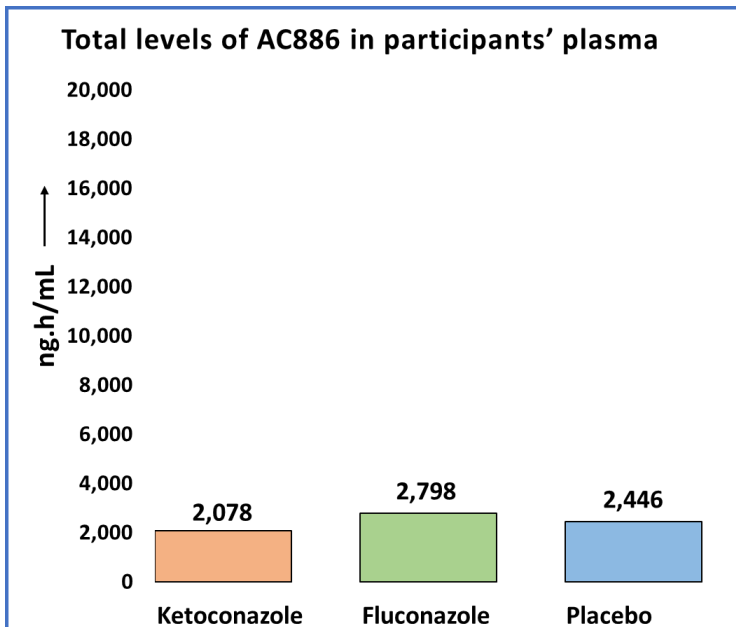
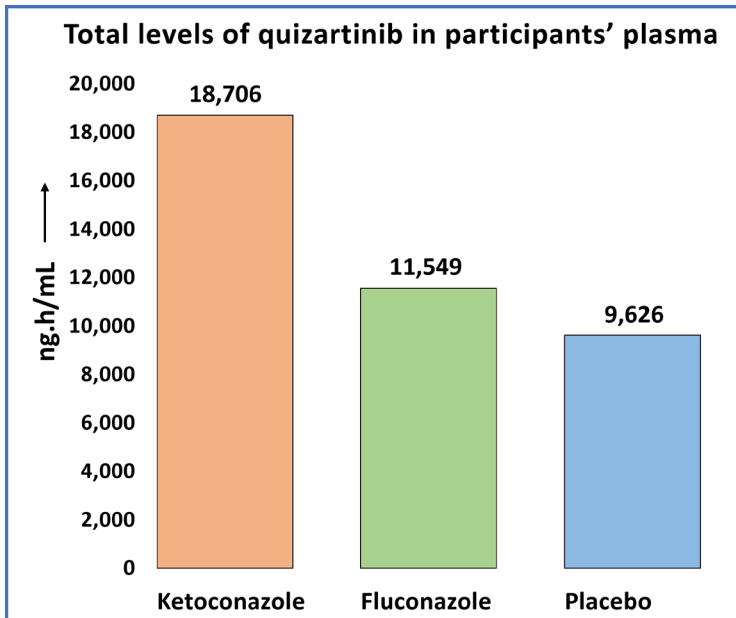
Key results from this study are shown for each group of participants as average results. This summary does not show the results from each individual participant. An individual participant's results could be different from the total group of participants.

What was the effect of ketoconazole and fluconazole on the plasma levels of quizartinib and its active breakdown product AC886 in healthy participants?

To answer this question, the researchers collected blood samples from the participants at defined timepoints over a period of time. They measured the levels of quizartinib and AC886 in the participants' plasma during the study.

Over time, participants who took quizartinib with ketoconazole had higher levels of quizartinib and slightly lower levels of AC886 in their plasma compared to participants who took quizartinib and placebo.

Participants who took quizartinib with fluconazole had similar levels of quizartinib and AC886 in their plasma compared to participants who took quizartinib and placebo.



What were the other results of this study?

What side effects did the participants develop during the study?

Side effects are medical problems that happened during the study, which the study doctor (investigator) 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.

Side effects other than those related to study treatment* are not reported here.

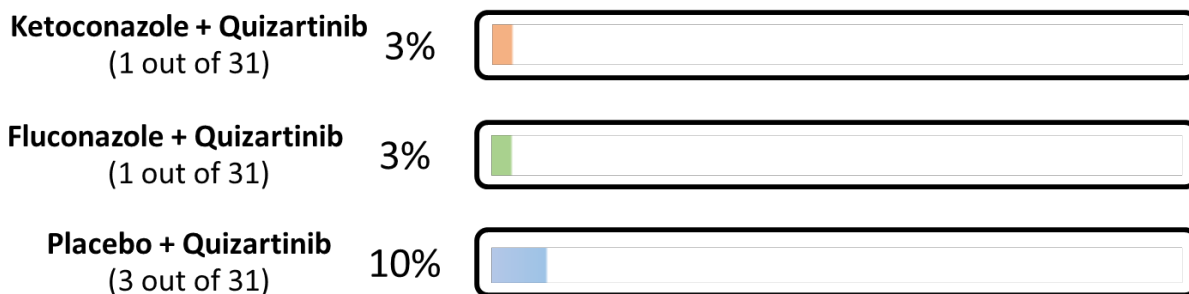
**If a side effect occurred before Day 8, the study treatment was ketoconazole or fluconazole. If the side effect occurred on or after Day 8, the study treatment was ketoconazole and quizartinib or fluconazole and quizartinib or placebo and quizartinib. Placebo looks like the study treatment but does not have any medicine in it.*

There were no serious side effects or deaths reported during this study. None of the participants in the study stopped treatment early because of side effects.

How many participants had side effects?

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

Percentage of Participants who had Side Effects



Side effects	Ketocanazole + Quizartinib (31 participants)	Fluconazole + Quizartinib* (31 participants)	Placebo + Quizartinib* (31 participants)
Change in bowel habit	0	1 (3%)	0
Decreased appetite	0	0	1 (3%)
Diarrhea	0	0	1 (3%)
Difficulty sleeping	0	0	1 (3%)
Feeling nervous and anxious	0	0	1 (3%)
Feeling sick to the stomach	1 (3%)	0	0
Cold sores	0	0	1 (3%)
Piles (Hemorrhoids)	0	1 (3%)	0
Weakness	0	0	1 (3%)

* 3 participants in the placebo + quizartinib group had 6 different side effects between them and 1 participant in the fluconazole + quizartinib group had 2 different side effects.

How was this study useful for patients and researchers?

This study helped researchers understand the effect of ketoconazole and fluconazole on the plasma levels of quizartinib and its breakdown product AC886 in healthy participants. The study results also helped inform researchers of the effects of drugs similar to ketoconazole and fluconazole on quizartinib and AC886 plasma levels.

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, randomized, placebo controlled, parallel group study to evaluate the effect of ketoconazole and fluconazole on the pharmacokinetics of quizartinib and its active metabolite, AC886, in healthy volunteers.

Sponsor: Daiichi Sankyo, Inc.

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