



Daiichi-Sankyo

## Clinical Results Summary

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

Protocol number: AC220-012

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 a study 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 is a drug already available in the market for treating fungal infections. Ketoconazole blocks a protein in the liver called CYP3A4 that breaks down quizartinib in the body. Taking both ketoconazole and quizartinib drugs together may slow down the breakdown of quizartinib in the body.

Rifampin is an antibiotic already available in the market for treating bacterial infections. Rifampin increases the activity of CYP3A4. Taking both rifampin and quizartinib drugs together may speed up the breakdown of quizartinib in the body.

Before a new drug can be given to patients, the researchers developing it perform many research studies to check that the drug is safe and effective when given alone or with other drugs. The first step in studying a new drug is to test it in healthy people. This means people without any health problems.

In this study, researchers wanted to understand the effects of ketoconazole and rifampin 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:



**Quizartinib**  
(Investigational drug)

An investigational drug being tested for the treatment of AML.



**Placebo**

A placebo looks like the study treatment and is given in the same way, but does not have any medicine in it.



**Ketoconazole**

An approved drug for treating fungal infections.



**Rifampin**

An approved drug for treating bacterial infections.

## Main purpose of this study

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



What is the effect of ketoconazole and rifampin on the plasma levels of quizartinib and its active breakdown product AC886\*?

*\*The body breaks down quizartinib into another product called AC886. AC886 has similar effects in the body to quizartinib.*

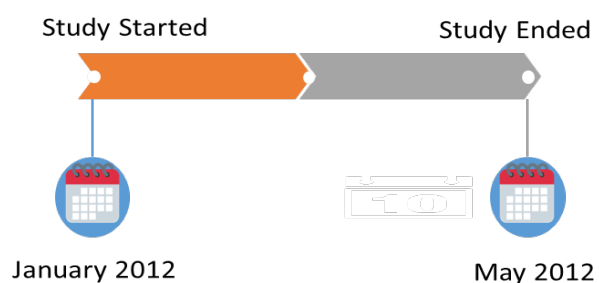
## Other purpose of this study

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 1 month.

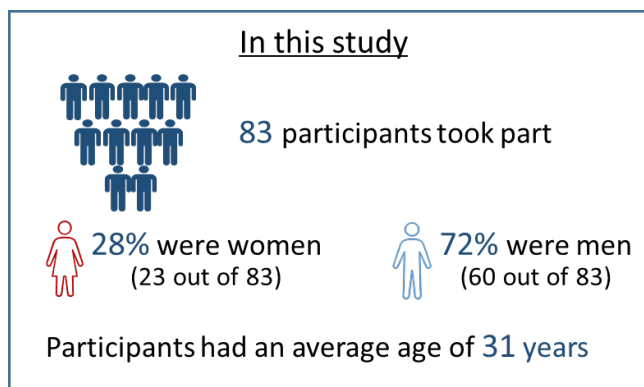
The study was completed as planned and a study report was created. This summary is based on that report.

## Who was in this study?

This study included 83 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,
- were using effective birth control methods during the study or were unable to have children,
- did not have major surgery within 90 days before treatment with quizartinib,
- had normal healthy kidneys and liver as measured by different blood tests,
- were able to communicate in English, and
- were able to follow the study requirements.



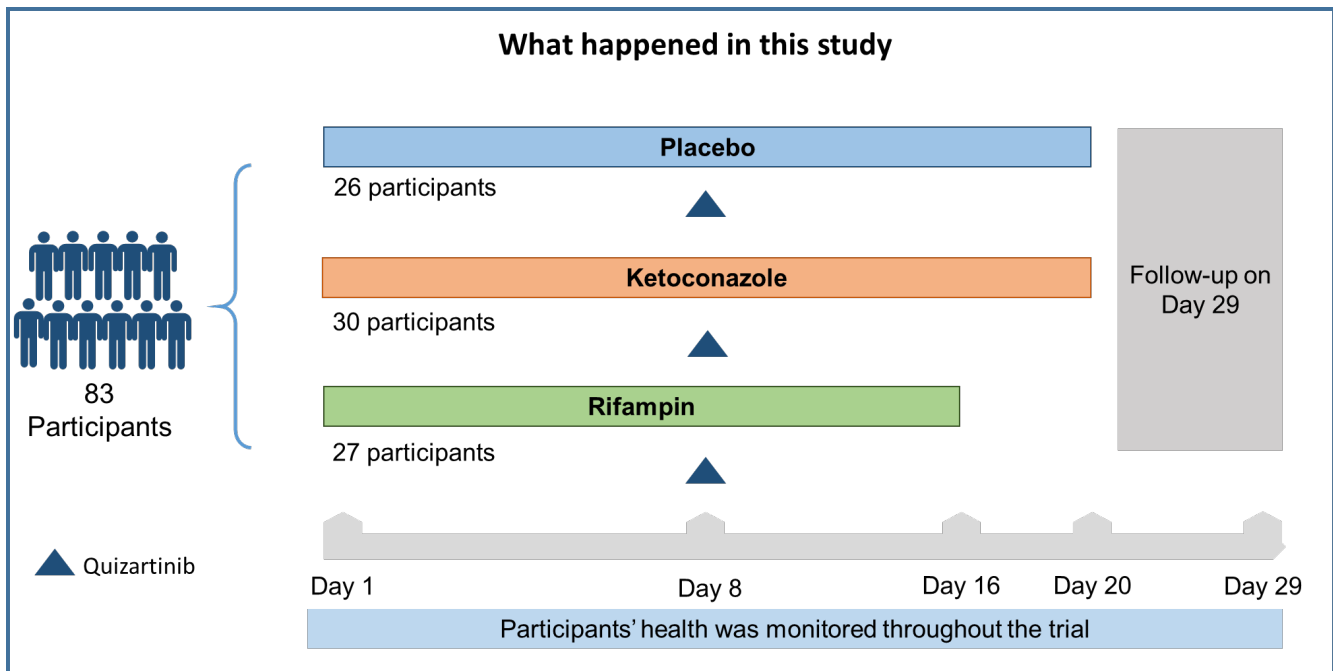
## What happened during this study?

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 and rifampin change the effect.

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

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

Participants were assigned to either placebo, ketoconazole or rifampin treatment group. Participants took placebo or ketoconazole every day from Day 1 to Day 20. Participants took rifampin every day from Day 1 to Day 16. On Day 8 only, participants in all 3 treatment groups also took a single dose of quizartinib.



## What were the key results of this study?

### What was the effect of ketoconazole and rifampin on the plasma levels of quizartinib and its active breakdown product AC886?

The blood samples from this study were not properly processed. Therefore it was not possible to accurately measure the effects of ketoconazole and rifampin on the plasma levels of quizartinib and its active breakdown product AC886. The effect of ketoconazole on the plasma levels of quizartinib was repeated in another study, AC220-015.

## What were the other results of this study?

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

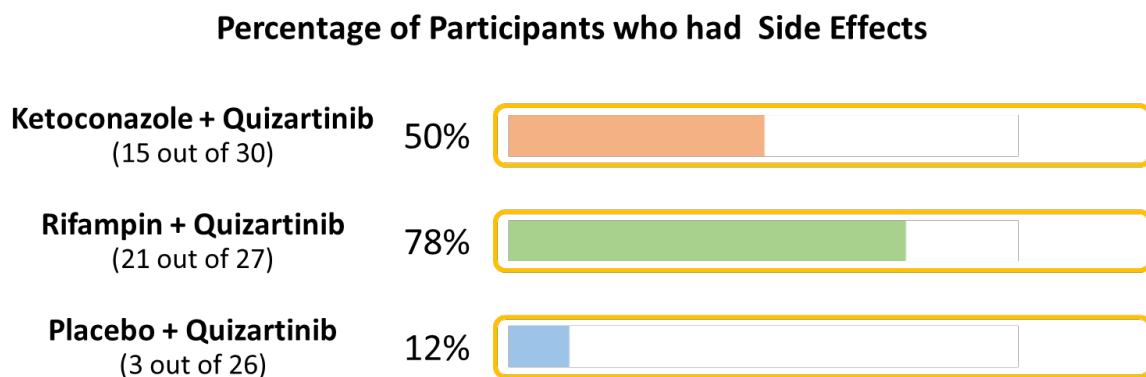
Side effects are medical problems that happened during the study which the study doctor (investigator) thought could be related to the treatments in the study. This section provides a summary of side effects related to the study treatments.

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.

No participant had a serious side effect during this study. No deaths were reported due to side effects.

### How many participants had side effects?

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



The most common side effects, which happened in more than 3 participants overall are presented below.

Side effects	Ketoconazole + Quizartinib 30 participants	Rifampin + Quizartinib 27 participants	Placebo + Quizartinib 26 participants
Abnormal urine color	0	21 (78%)	0
Decrease in appetite	1 (3%)	3 (11%)	0
Diarrhea	0	4 (15%)	0
Feeling tired	1 (3%)	2 (7%)	1 (4%)
Headache	6 (20%)	5 (18%)	1 (4%)
Itching	1 (3%)	2 (7%)	0
Nausea	8 (27%)	1 (4%)	1 (4%)
Stomach pain	2 (7%)	0	1 (4%)

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

During the study, 3 out of 30 (10%) participants in the ketoconazole and quizartinib group and 1 out of 27 (4%) participants in rifampin and quizartinib group stopped treatment due to side effects. If the side effect occurred before Day 8, the treatment was ketoconazole or rifampin. If the side effect occurred on or after Day 8, the treatment was ketoconazole and quizartinib or rifampin and quizartinib. No participants in the placebo and quizartinib group stopped treatment due to side effects.

The side effects that caused 3 participants in the ketoconazole and quizartinib group to stop treatment were:

- anal pain
- skin allergy, tightness in throat and difficulty in breathing
- skin reaction to the treatment

One participant in the rifampin and quizartinib group stopped rifampin and quizartinib treatment due to decreased neutrophil count. Neutrophils are a type of white blood cell that fight bacteria.

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

This study was designed to help researchers understand the effect of ketoconazole and rifampin on the plasma levels of quizartinib and its breakdown product AC886 in healthy participants. However, it was not possible to determine this because of an issue with blood sample processing during the study.

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 Rifampin on the Pharmacokinetics of AC220 and its Active Metabolite, AC886, in Healthy Volunteers

**Sponsor:** Daiichi Sankyo, Inc.

**Sponsor contact information:**

211 Mount Airy Road, Basking Ridge, NJ 07920

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

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

**Date of this summary:** 15 February 2022

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