NOVARTIS

Clinical Trial Results Summary

A trial to learn how KAE609 affected liver health and about its safety in participants with malaria

Trial Number: CKAE609A2202

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug KAE609. All of the participants helped the researchers learn more about how KAE609 works and how safe it is to take.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

If you participated in the trial and have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the websites listed on the last page of this summary.

Overview of this trial and the results

What was the purpose of this trial?

In this clinical trial, the researchers studied how a trial drug called KAE609 affected the liver health of participants with malaria. The researchers also studied the safety of KAE609 in these participants.

The main questions the researchers wanted to answer in this trial were:

- How many of the participants' liver health changed after taking KAE609?
- What medical problems happened during this trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of KAE609.

Another question the researchers wanted to answer was:

- How did trial treatment affect the participants' malaria infections?

Who was in this trial?

There were 188 men and women who had malaria that participated in this clinical trial.

What treatments did the participants take?

The participants in this trial took either KAE609 or a malaria treatment called Coartem®, also known as artemether lumefantrine tablets. Coartem® is already approved to prescribe for patients with malaria.

What were the main results of the trial?

Overall, the researchers learned that:

- The number of participants with a change in their liver health was similar in the participants who took KAE609 and those who took Coartem®. The researchers found that 1.5% of the participants who took KAE609 had their liver health worsen after taking treatment. This was 2 out of 135 participants. They found that 3.9% of participants who took Coartem® had their liver health worsen. This was 2 out of 51 participants.

More details about the results of this trial are included later in this summary.

What was the purpose of the trial?

Researchers are looking for a different way to treat malaria. Before a trial drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works. KAE609 is being developed as a possible treatment for malaria.

Malaria is a serious disease that is spread by mosquitos that are infected by a "parasite". A parasite is an organism that lives on or in another living thing and causes it harm.

Malaria is caused when an infected mosquito bites a person and transfers the parasite into the person's blood. The symptoms of malaria can include fever, headache, vomiting, diarrhea, muscle pain, feeling hot, and having chills. If malaria is not treated quickly, it can lead to more serious conditions like having a very low number of red blood cells, seizures, and brain damage.

There are treatments already available for malaria, but these may not help all patients. The trial treatment, KAE609, works by blocking a specific protein that is found on certain cells of the parasite in the blood. Researchers think that stopping this protein from working may help kill the parasite in the blood.

In another trial with KAE609, some of the participants' liver health got worse after they took KAE609. In this trial, the researchers wanted to learn more about if KAE609 affected the participants' liver health compared to a malaria treatment called Coartem®. They also wanted to compare the safety of KAE609 with the safety of Coartem®. Coartem® is already approved for doctors to prescribe to patients with malaria.

The main questions the researchers wanted to answer in this trial were:

- How many of the participants' liver heath changed after taking KAE609?
- What medical problems happened during this trial?

Another question the researchers wanted to answer was:

- How did the trial treatment affect the participants' malaria infections?

Who was in this trial?

To answer the questions in this trial, the researchers asked for the help of men and women who had malaria.

Everyone in this trial was 18 to 61 years old when they joined the trial.

The trial included 188 African participants in Gabon (16 participants), Ghana (29 participants), Mali (11 participants), Rwanda (74 participants), and Uganda (58 participants).

What treatments did the participants take?

The participants in this trial took KAE609 or Coartem® as capsules or tablets by mouth. Coartem® is made up of 2 different drugs called artemether and lumefantrine.

The doses were measured in milligrams, also known as mg. The participants who took KAE609 took 1 of 5 different doses.

The researchers used a computer program to randomly choose the treatment each participant took. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible.

During this trial, each participant knew what they were taking. The trial staff and sponsor staff also knew what each participant was taking.

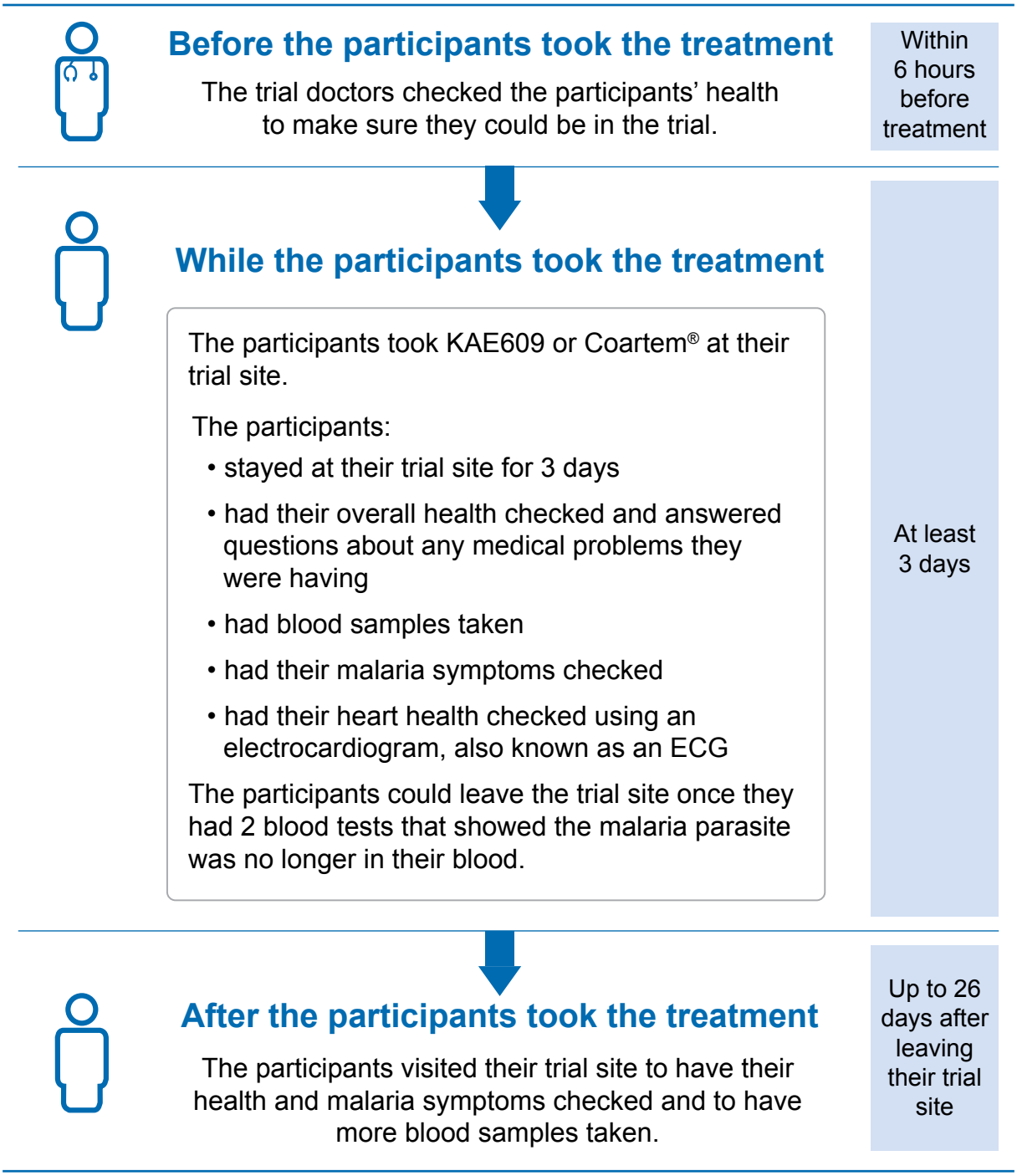
The chart below shows the treatments that each group of participants took:

KAE609	Coartem®
• As capsules by mouth	• As tablets by mouth
• Either 1 single dose or once a day for 3 days	• Twice a day for 3 days
• 10 participants took 10 mg of KAE609 1 time • 10 participants took 10 mg of KAE609 once a day for 3 days • 12 participants took 25 mg of KAE609 1 time • 20 participants took 25 mg of KAE609 once a day for 3 days • 22 participants took 50 mg of KAE609 1 time • 20 participants took 50 mg of KAE609 once a day for 3 days • 21 participants took 75 mg of KAE609 1 time • 22 participants took 150 mg of KAE609 1 time	• 51 participants took coartem® • Coartem® is made up of 80 mg of artemether and 480 mg of lumefantrine

What happened during this trial?

The trial started in November 2017 and ended in November 2019. Each participant was in the trial for up to 29 days.

The chart below shows what happened during the trial.



What were the main results of this trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making changes to your healthcare.

There were 2 participants who did not receive the trial treatment. So, the results below only include 186 participants.

How many of the participants' liver health changed after taking KAE609?

Overall, the researchers found that the number of participants with a change in their liver health was similar in the participants who took KAE609 and those who took Coartem®.

The researchers wanted to know how many of the participants' liver health changed after taking KAE609. To find this out, the trial doctors took blood from the participants before the participants took trial treatment, and throughout the trial. In the participants' blood, they measured the level of:

- alanine aminotransferase, also known as ALT
- aspartate transaminase, also known as AST

High levels of ALT and AST in the blood can be a sign of liver damage.

The researchers compared the levels of ALT and AST in the participants' blood before they took the trial treatments and at different times during the trial. If the participants' ALT or AST levels had increased by a certain amount, this meant that their liver health had worsened.

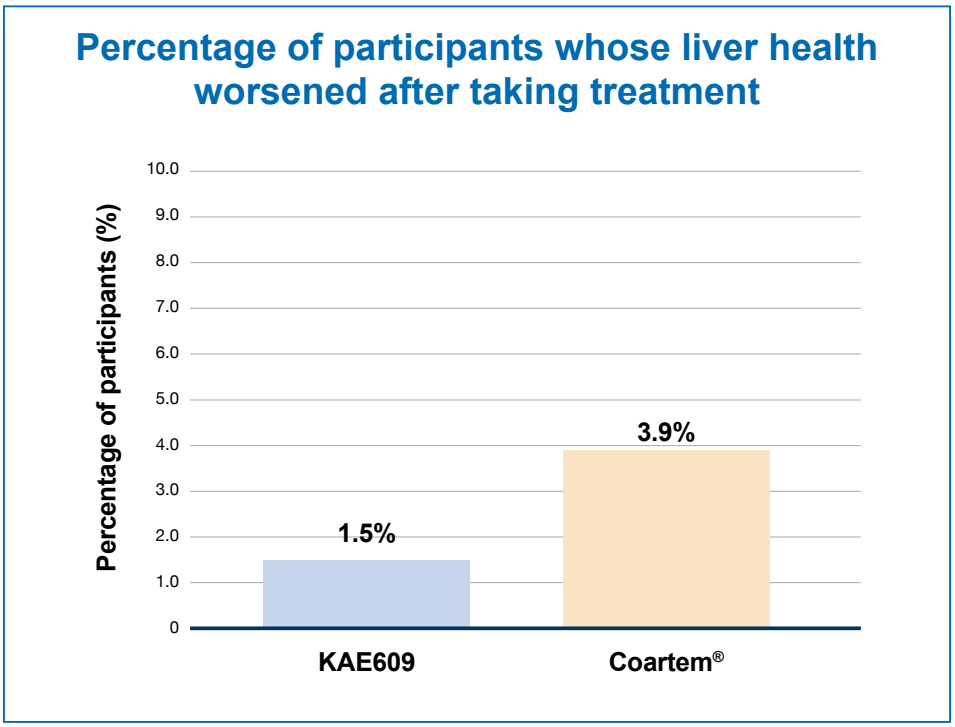
They combined the results of all the participants who took KAE609. Then, they compared this with the results for the participants who took Coartem®.

Overall, the researchers found that:

- 1.5% of participants who took KAE609 had their liver health worsen. This was 2 out of 135 participants.
- 3.9% of participants who took Coartem® had their liver health worsen. This was 2 out of 51 participants.

Although the results for the participants who took Coartem® was higher than those who took KAE609, the difference between the treatments was too small for the researchers to know if Coartem® changed the participants' liver health more than KAE609. The difference could have been due to chance.

The chart below shows these results.



What other results were learned?

How did the trial treatment affect the participants' malaria infections?

The researchers wanted to learn how the trial treatments affected the participants' malaria infections. To find this out, the trial doctors took blood samples before the participants took trial treatment and throughout the trial. It is important to know this was not the main question the researchers wanted to answer.

The researchers studied:

- the number of participants who cleared the parasite from their blood by Day 15 through to Day 29
- the average number of hours it took to clear the parasite from the blood
- the average number of hours it took to clear a fever in the participants who had a fever before taking trial treatment
- the number of participants who had their malaria infection come back at Day 29

Overall, the researchers found that:

- **Most of the participants who took KAE609 or Coartem® cleared the parasite from their blood by Day 29.**
- **The participants who took KAE609 cleared the parasite in their blood in a shorter amount of time compared to those who took Coartem®.**
- **Too few participants had a fever before taking the trial treatment for the researchers to calculate the average number of hours to clear a fever.**
- **More participants who took KAE609 had their malaria infection come back at Day 29 compared to the participants who took Coartem®.**

What medical problems happened during this trial?

Medical problems that happen in clinical trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An **adverse event** is considered “serious” when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death.

Adverse events may or may not be caused by the treatments in the trial. A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

This section is a summary of the adverse events that happened during this trial.

73.1% of the participants had adverse events during this trial. This was 136 out of 186 participants. Some of the adverse events were serious. None of the participants left the trial due to an adverse event.

Summary of adverse events

Treatment group	Participants who had any adverse events (Percentage and number of participants)	Participants who had serious adverse events (Percentage and number of participants)
10 mg of KAE609 1 time	90.0% 9 of 10	0.0% 0 of 10
10 mg of KAE609 once a day for 3 days	80.0% 8 of 10	0.0% 0 of 10
25 mg of KAE609 1 time	83.3% 10 of 12	0.0% 0 of 12
25 mg of KAE609 once a day for 3 days	70.0% 14 of 20	0.0% 0 of 20
50 mg of KAE609 1 time	66.7% 14 of 21	0.0% 0 of 21
50 mg of KAE609 once a day for 3 days	84.2% 16 of 19	5.3% 1 of 19
75 mg of KAE609 1 time	90.5% 19 of 21	9.5% 2 of 21
150 mg of KAE609 1 time	59.1% 13 of 22	4.5% 1 of 22
Coartem®	64.7% 33 of 51	2.0% 1 of 51

None of the participants left the trial due to adverse events.

What were the serious adverse events?

The serious adverse events that happened during the trial were:

- **Low levels of a type of blood cell called platelets** happened in 1 out of 21 participants who took **75 mg of KAE609 1 time** (4.8% of the participants).
- **Increased levels of alanine aminotransferase in the blood (a sign of liver damage)** happened in 1 out of 22 participants who took **150 mg of KAE609 1 time** (4.5% of the participants).
- **Increased levels of alkaline phosphatase in the blood (a sign of liver damage)** happened in 1 out of 21 participants who took **75 mg of KAE609 1 time** (4.8% of the participants).
- **Increased levels of bilirubin in the blood (a sign of liver damage)** happened in 1 out of 19 participants who took **50 mg of KAE609 once a day for 3 days** (5.3% of the participants) and in 1 out of 51 participants who took **Coartem®** (2.0% of the participants).

No other serious adverse events were reported. None of the participants died due to serious adverse events during this trial.

What were the non-serious adverse events?

The table below shows the adverse events that happened in at least 20.0% of the participants in any treatment group. There were other adverse events, but these happened in fewer participants.

	Adverse event		
Treatment group	**Being infected with malaria a second time** (Percentage and number of participants)	**Headache** (Percentage and number of participants)	**Parasites not being cleared from the participants' blood** (Percentage and number of participants)
10 mg of KAE609 1 time	**10.0%** 1 of 10	**30.0%** 3 of 10	**0.0%** 0 of 10
10 mg of KAE609 once a day for 3 days	**0.0%** 0 of 10	**50.0%** 5 of 10	**10.0%** 1 of 10
25 mg of KAE609 1 time	**16.7%** 2 of 12	**8.3%** 1 of 12	**25.0%** 3 of 12
25 mg of KAE609 once a day for 3 days	**20.0%** 4 of 20	**5.0%** 1 of 20	**5.0%** 1 of 20
50 mg of KAE609 1 time	**19.0%** 4 of 21	**9.5%** 2 of 21	**0.0%** 0 of 21
50 mg of KAE609 once a day for 3 days	**26.3%** 5 of 19	**10.5%** 2 of 19	**5.3%** 1 of 19
75 mg of KAE609 1 time	**23.8%** 5 of 21	**23.8%** 5 of 21	**0.0%** 0 of 21
150 mg of KAE609 1 time	**40.9%** 9 of 22	**0.0%** 0 of 22	**0.0%** 0 of 22
Coartem®	**2.0%** 1 of 51	**17.6%** 9 of 51	**3.9%** 2 of 51

For information about the adverse events in this trial, please see the complete technical summary that can be found on the website noted at the end of the summary.

What was learned from this trial?

The information described above helped the researchers learn more about how KAE609 affected liver health in participants with malaria. **The researchers looked at how many of the participants' liver health changed after taking KAE609. Overall, the researchers found that the number of participants with a change in their liver health was similar in the participants who took KAE609 and those who took Coartem®.**

The results presented here are for a single trial. This summary shows only the main results from this one trial. If you have any questions, please talk to the doctor or staff at your trial site.

Further clinical trials with KAE609 are planned. This includes a trial where KAE609 will be used with another treatment in participants with malaria.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website.

- Go to www.novctrd.com.
- Once on the site, click **"Clinical Trial Results"** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **"Study number"** from the drop-down menu.
- Type **"CKAE609A2202"** into the keyword search box and click **"Search"**.

If you would like to view the website in a language other than English, you can click the **"Google Translate"** button on the top right of the page.

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CKAE609A2202"** into the **"Other terms"** search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or at www.novartisclinicaltrials.com. Search for **"KAE609"** or **"Malaria"**.

Full trial title: A Phase 2, multi-center, randomized, open-label, dose-escalation study to determine safety of single (QD) and multiple (3 QD) doses of KAE609, given to adults with uncomplicated Plasmodium falciparum malaria

Protocol number: CKAE609A2202

Thank you!

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study new medical treatments.

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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