NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of COA566 in newborns and young babies with malaria who weigh less than 5 kilograms

Thank you!

Thank you to the babies and their families who took part in the clinical trial for malaria. Every participant helped the researchers learn more about the trial drug **COA566**, also called **artemether-lumefantrine**.

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.

Trial information

Trial number: CCOA566B2307
Novartis drug studied: **COA566**, also called artemether-lumefantrine
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn more about the effects of **COA566** in newborns and young babies with malaria. There are no approved treatments for malaria in young babies who weigh less than 4.5 kilograms (kg), even though these young babies may get malaria.

Malaria is a disease caused by a parasite called plasmodium. Malaria spreads to people through the bite of an infected mosquito. The parasite enters the blood and infects red blood cells. It can also spread to an unborn baby during pregnancy or a newborn during childbirth.

In babies, malaria can cause fever, cough, being irritable, trouble sleeping, and not eating well. Malaria is more likely to become severe in children younger than 5 years.

COA566, also called artemether-lumefantrine is a trial drug designed to treat malaria. It is a combination of 2 drugs:

- **Artemether**, which kills the malaria parasite quickly
- **Lumefantrine**, which kills the parasite more slowly for a longer time

By combining these 2 drugs, **COA566** starts killing the parasite quickly and continues to kill it over time.

COA566 is approved in some countries to treat malaria in adults and babies who weigh 5 kg or more. In this trial, researchers wanted to find a dose to use with babies who weigh less than 5 kg.

Trial drug
COA566 also called artemether-lumefantrine

Pronounced as
ar-teh-meth-er loo-meh-fan-treen

The trial's purpose was to answer these main questions:

- What was the highest blood level of artemether 1 or 2 hours after the first dose?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

Why did researchers only look at levels of artemether?

In a **past trial**, COA566B2306, babies with malaria were given 20 mg of **artemether** and 120 mg **lumefantrine**. Researchers found that at those doses:

- **Artemether** reached higher levels in the blood than expected in small babies
- **Lumefantrine** stayed at expected levels in small babies

In this trial, researchers gave a lower dose of **artemether** to small babies to learn if it stayed within the target range. To measure this, they looked at the blood levels of **artemether** 1 or 2 hours after the first dose.

How long was this trial?

The trial began in December 2020 and ended in May 2024. The babies were in the trial for up to 1 year.

The sponsor decided to stop recruitment early due to difficulty in finding babies one month or younger to join the trial. The decision was not due to safety concerns or how well the trial drug worked. Babies who were already in the trial continued as planned.

Who was in this trial?

28 babies with malaria received treatment in this trial – 10 boys and 18 girls. The babies' ages ranged from 1 day to 6 months. Their average age was about 3 months.

The number of participants by race is shown below.

Race

28	Black or African

The babies could take part in this trial if they:

- Weighed at least 2 kg, but less than 5 kg
- Had malaria based on a blood test, with or without symptoms
- Had malaria that wasn't severe

28 babies from 2 countries received treatment. The babies took part in:

- Burkina Faso | 7 babies
- Democratic Republic of the Congo | 21 babies

What treatments did the babies receive?

The treatment in this trial was:

COA566, also called **artemether-lumefantrine**, which was taken by mouth 2 times a day for 3 days. Tablets of **COA566** were dissolved into water and given to the babies using a syringe before or after the baby was fed.

The dose of **COA566** in this trial was:

- 5 milligrams (mg) **artemether**
- 60 mg **lumefantrine**

The families, researchers, and trial staff knew what treatment each baby received. All babies received **COA566**.

What happened during this trial?

Before treatment — **1 day**

Trial staff checked to make sure the babies could be in this trial.

During treatment — **3 days**

Trial staff assigned the 28 babies to a group based on their age:

- **Group 1** (older than 1 month): 22 babies
- **Group 2** (1 month or younger): 6 babies

The babies in each group received **COA566** by mouth 2 times a day for 3 days.

Trial doctors started by giving a dose of 5 mg of **artemether** and 60 mg **lumefantrine** to the first few babies in Group 1.

Trial doctors could change the dose if they had concerns about safety or effects on malaria.

Because trial doctors had no concerns about the dose's safety or effects, they gave all babies 5 mg of **artemether** and 60 mg **lumefantrine**.

After treatment — **Until the baby turned 1 year old**

Trial staff checked the babies for:

- Any medical problems for up to 6 weeks after their first dose of trial treatment
- Serious medical problems until the baby turned 1 year old

Trial staff checked the babies' general health throughout the trial. Each baby's family member or caregiver went to trial visits with them.

What were the main results of this trial?

What was the highest blood level of artemether 1 or 2 hours after the first dose?

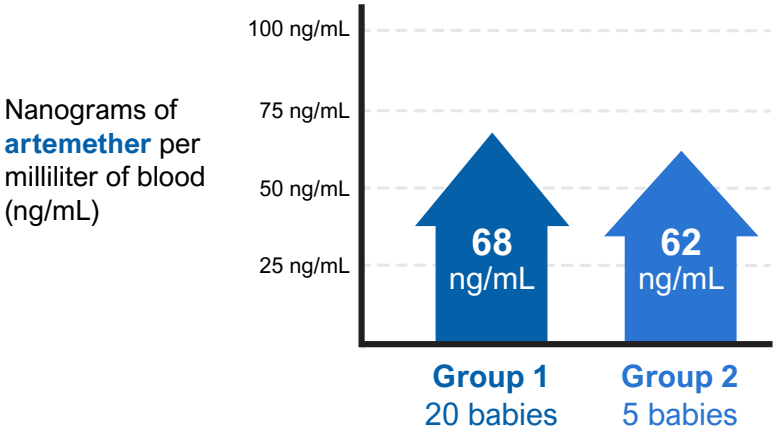
On average, the highest blood level of **artemether** in both groups was between 60 and 70 nanograms per milliliter (ng/mL) of blood, which was within the target range.

To learn this, researchers measured the level of **artemether** in the blood samples at 1 and 2 hours after each baby received their first dose of **COA566**. They looked at whichever sample had the higher level of drug to see if that level was within the **target range**.

How did researchers choose the target range?

Researchers chose the target range of **artemether** that would be safe for small babies and could work to treat malaria based on the results from the past trial **COA566B2303**.

Average highest blood level of artemether 1 or 2 hours after the first dose



This graphic does not include babies whose blood samples could not be used for results.

What were the other results of this trial?

How many babies had the malaria parasite come back or a new malaria infection within 6 weeks after starting treatment?

In **Group 1** (older than 1 month), the researchers concluded:

- 2 of 22 babies had the malaria parasite come back within 6 weeks after starting trial treatment
- 6 of 22 babies had a new malaria infection within 6 weeks after starting trial treatment

In **Group 2** (1 month or younger), no babies had the malaria parasite come back or a new malaria infection within 6 weeks after starting treatment.

How long did it take for the babies' malaria parasites to go away?

In **Group 1** (older than 1 month), the researchers concluded it took about **35 hours** for the malaria parasite in the babies' blood to go away.

In **Group 2** (1 month or younger), the researchers concluded it took about **31 hours** for the malaria parasite in the babies' blood to go away.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until:

- The baby turned 1 year old for serious adverse events
- Up to 6 weeks after the start of treatment for other adverse events

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- 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 treatments in the trial.

Most of the babies (21 of 28) had adverse events that were similar to past trials of **COA566** in older babies who weighed more than 5 kg. No babies had adverse events that were considered serious, and none died. No babies left the trial due to an adverse event. The researchers concluded there were no new safety concerns for **COA566** in this trial.

How many babies had adverse events?

Babies who:	Group 1 22 babies	Group 2 6 babies
Had at least 1 **serious adverse event**	**0 of 22** 0%	**0 of 6** 0%
Had at least 1 **other adverse event**	**17 of 22** 77%	**4 of 6** 67%

What serious adverse events did the babies have?

No babies had serious adverse events, and none died.

What other adverse events did the babies have?

21 babies had other adverse events.

The table below shows the other adverse events that happened in **2 or more** babies. Additional adverse events happened in fewer babies.

	Group 1 22 babies	Group 2 6 babies
Fever Pyrexia	8 of 22 36%	2 of 6 33%
Malaria that came back Malaria	9 of 22 41%	0 of 6 0%
Low levels of red blood cells Anemia	7 of 22 32%	1 of 6 17%
Throwing up Vomiting	6 of 22 27%	1 of 6 17%
A bacterial infection in the nose and sinuses Bacterial rhinitis	2 of 22 9%	0 of 6 0%

What was learned from this trial?

Researchers learned more about the effects **COA566** in newborns and young babies with malaria. The sponsor ended recruitment early due to difficulty finding babies 1 month or younger to join the trial.

The researchers concluded that:

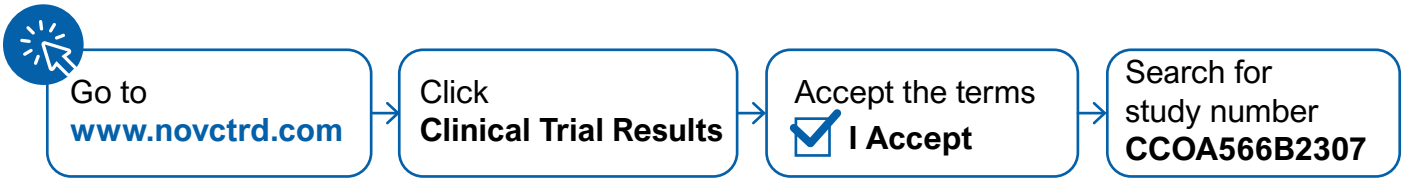
- On average, the highest blood level of **artemether** in both groups was within the target range
- These results were similar to those from the past trial COA566B2303:
  - The number of babies who had the malaria parasite come back or had a new malaria infection within 6 weeks
  - The length of time for the malaria parasite in the babies' blood to go away
- There were no new safety concerns for **COA566** in this trial

When this summary was written, the sponsor had no plans for future trials of **COA566** in people with malaria.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:



For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT04300309**

Other trials of **COA566** may appear on the public website above. When there, search for **COA566**, or **artemether-lumefantrine**.

Full clinical trial title: Multicenter, open-label, single-arm study to evaluate the PK, safety, tolerability and efficacy of a new artemether:lumefantrine (2.5 mg:30 mg) dispersible tablet in the treatment of infants and neonates <5 kg body weight with acute uncomplicated Plasmodium falciparum malaria

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1-888-669-6682 (US) | +41-61-324 1111 (EU)

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