

**Research Sponsor:** Novartis

**Drug Studied:** LIK066

**Protocol Number:** CLIK066X2205

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## ***Thank you!***

Thank you to the participants who took part in the clinical trial for LIK066. All of the participants helped researchers learn more about how LIK066 works in people with polycystic ovary syndrome, also known as PCOS.

Novartis sponsored this trial and believes it is important to share the results of the trial with the participants and the public. An independent non-profit organization called CISC RP prepared this summary of the trial results. We hope it 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.

## **What has happened since the trial ended?**

The participants were in the trial for a little over 2 months. But, the whole trial took about 11 months to finish. This is because the participants started and stopped treatment at different times. The trial started in July 2017 and ended in June 2018.

The trial included a total of 29 participants in Germany and the United States. After the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

## **Why was the research needed?**

Researchers are looking for another way to treat PCOS. Before a new drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works.

Women with PCOS have an imbalance in sex hormones. This can cause irregular periods, problems with pregnancy, and other health problems. An imbalance in sex hormones can affect other hormones and proteins in the body. One of these hormones is insulin, which decreases the level of sugar in the blood. This sugar is also known as glucose.

Women with PCOS often have high levels of insulin. Weight gain and obesity can increase insulin levels even higher. High levels of insulin can affect the levels of certain sex hormones in the body, like testosterone. Because of this, doctors often treat PCOS with a medicine that decreases insulin and blood glucose.

In this trial, the researchers wanted to learn more about LIK066. This trial drug decreases the amount of glucose taken in from food. It also increases the amount of glucose that the kidneys remove from the body. In this trial, the researchers compared LIK066 to a placebo. A placebo looks like the trial drug but does not have any medicine in it. Using a placebo helps researchers better understand the actual effect of the trial drug.

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

- Did LIK066 reduce testosterone levels in the blood?
- Did LIK066 change the levels of other hormones and proteins in the blood?
- What medical problems did the participants have?

To answer the questions in this trial, the researchers asked for the help of women with PCOS. These women were overweight or had obesity and higher levels of insulin. The women in the trial were 19 to 39 years old when they joined.

## What kind of trial was this?

In this trial, the participants took either LIK066 or the placebo. The researchers used a computer program to randomly choose the treatment each participant took. Doing a trial this way helps make sure the results are looked at fairly.

This trial was “double-blind”. This means none of the participants, trial doctors, trial staff, or sponsor staff knew what treatment each participant took. Some trials are done this way because knowing what treatment the participants are taking can affect the results of the trial.

When the trial ended, the sponsor found out which treatment each participant took so they could create a report of the results. The sponsor staff did not know the identity of any of the participants.

## What happened during the trial?




**Before the treatment started**, the trial doctors did tests to make sure the participants could take part in the trial. This part lasted between 1 and 6 weeks. The trial doctors:

- checked the participants’ overall health
- asked participants what medicines they were taking
- took blood and urine samples
- checked the participants’ hormone and glucose levels

The trial doctors did these tests again during treatment.

**During treatment,** the participants took pills of either LIK066 or the placebo 3 times a day for 14 days. On Day 15, the participants took LIK066 or the placebo 1 time before breakfast. Doses of the trial drug were measured in milligrams, also called mg.

The chart below shows the treatments the participants took in this trial.

	<ul style="list-style-type: none"> <li>• 15 participants took 50 mg of LIK066.</li> <li>• 14 participants took the placebo.</li> </ul>
	<ul style="list-style-type: none"> <li>• The participants took LIK066 or the placebo by mouth.</li> </ul>
	<ul style="list-style-type: none"> <li>• The participants took LIK066 or the placebo 3 times a day for 14 days, before each meal. On Day 15, the participants took LIK066 or the placebo 1 time before breakfast.</li> </ul>

**After treatment ended,** the participants visited their trial site about 7 days after they took their last dose of LIK066 or the placebo. During this visit, the trial doctors checked the participants' health and took blood and urine samples.

## What were the results of the trial?

This is a summary of the overall results of the trial, not your individual results. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial. Always talk to a doctor before making any changes to your medications or treatment plans.

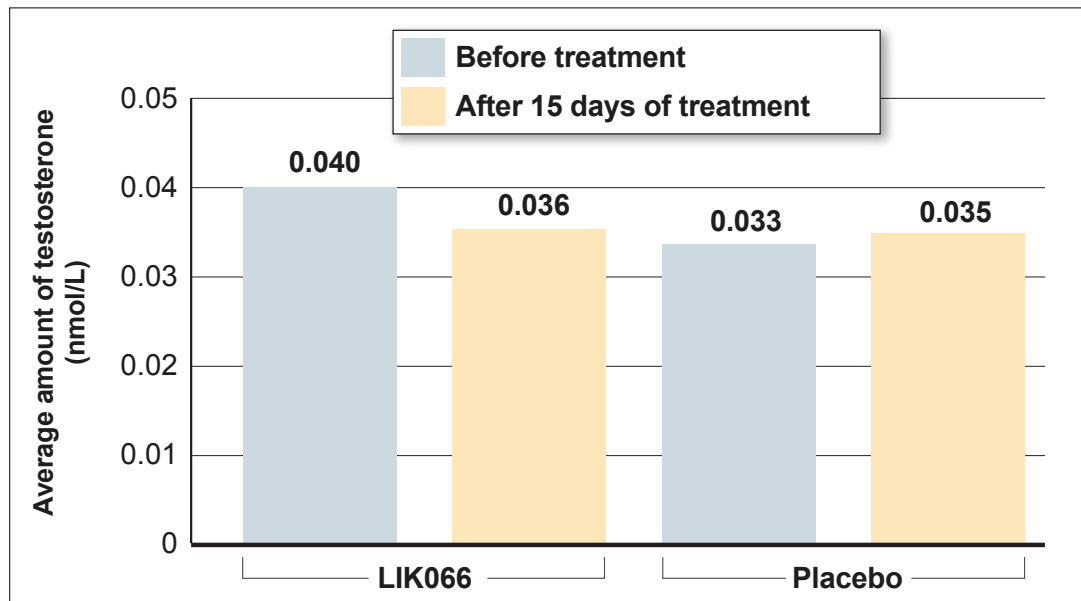
### Did LIK066 reduce testosterone levels in the blood?

To answer this question, the trial doctors took blood samples from the participants before the first dose of treatment and after 15 days of treatment. They measured the amount of testosterone in nanomoles per liter of blood, also known as nmol/L.

Overall, the researchers found that the participants who took LIK066 had slightly lower testosterone levels after 15 days of treatment. The participants who took the placebo had slightly higher testosterone levels after 15 days of treatment. But, the difference between the treatment groups was too small for researchers to conclude that LIK066 reduced testosterone levels in the blood.

The chart below shows the average amount of testosterone in the participants' blood before and after 15 days of treatment.

**Average amount of testosterone in the participants' blood**



### Did LIK066 change the levels of other hormones and proteins in the blood?

To answer this question, the trial doctors looked at samples of the participants' blood taken before treatment and after 15 days of treatment. They wanted to see if there was a change in the levels of other hormones and proteins that can be affected in women with PCOS.

Women with PCOS commonly have increased testosterone levels compared to women without PCOS. When testosterone levels are increased in women with PCOS, other hormones and proteins can also be affected.

Compared to participants who took the placebo, the researchers found that the level of these hormones and proteins changed in the participants who took LIK066. But, for most of the hormones and proteins tested, the difference between the treatment groups was too small for the researchers to conclude that LIK066 caused these changes.

The chart below shows the changes in the hormones and proteins that were measured after 15 days of LIK066 treatment compared to placebo.

Change in hormones and proteins after LIK066 treatment compared to placebo		
Hormone or protein	Role in PCOS	Change after 15 days of treatment
Androstenedione	A hormone that helps make testosterone from DHEA. High levels of androstenedione are a sign of PCOS.	Decreased by 18%.
Dehydroepiandrosterone (DHEA)	A hormone that the body can use to make testosterone or estrogen. High levels of DHEA are a sign of PCOS.	Decreased by 31%.
Dehydroepiandrosterone sulfate (DHEAS)	A hormone that is made when the body breaks down DHEA. High levels of DHEAS are a sign of PCOS.	Decreased by 24%.
Follicle stimulating hormone (FSH)	Hormone made and released by the brain's pituitary gland. Low levels of FSH are a sign of PCOS.	Increased by 27%.
Free androgen index (FAI)	The amount of testosterone that is available for the body to use. High levels of FAI are a sign of PCOS.	Decreased by 21%.
Luteinizing hormone (LH)	Hormone made and released by the brain's pituitary gland. High levels of LH are a sign of PCOS.	Increased by 25%.
Sex hormone binding globulin (SHBG)	Binds to hormones like testosterone. Once bound to the hormone, SHBG keeps it from interacting with the body. Low levels of SHBG are a sign of PCOS.	Increased by 15%.
Total testosterone	A sign of increased testosterone production in the ovaries is one of the main ways that PCOS is diagnosed in women.	Decreased by 9%.

## What medical problems did the participants have?

The researchers wanted to know what medical problems the participants had during the trial. They also wanted to know if the participants' health was affected in other ways during the trial.

Medical problems that happen in clinical trials are called "adverse events". An adverse event is any sign or symptom that participants have during a trial. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participants need hospital care.

These problems may or may not be caused by the trial drug. A lot of research is needed to know whether a drug causes a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that participants have.

## How many participants had adverse events?

In this trial, 86.2% of the participants in both treatment groups had adverse events. This was 25 of the 29 participants.

None of the participants stopped taking the trial drug because of an adverse event.

The table below shows how many participants in each treatment group had adverse events during this trial.

Adverse events during this trial			
	50 mg LIK066 (Out of 15 participants)	Placebo (Out of 14 participants)	Total (Out of 29 participants)
How many participants had adverse events?	100% (15)	71.4% (10)	86.2% (25)

## What were the serious adverse events?

None of the participants had serious adverse events during this trial.

None of the participants died during this trial.

## What were the most common adverse events?

The most common adverse event in this trial was diarrhea. This happened in 62.1% of the participants. This was 18 of the 29 participants.

The table below shows the adverse events that happened in 2 or more participants in this trial. There were other adverse events, but these happened in fewer participants.

<b>Adverse events during this trial</b>			
	<b>50 mg LIK066 (Out of 15 participants)</b>	<b>Placebo (Out of 14 participants)</b>	<b>Total (Out of 29 participants)</b>
Diarrhea	100% (15)	21.4% (3)	62.1% (18)
Nausea	33.3% (5)	14.3% (2)	24.1% (7)
Passing gas	40.0% (6)	0.0% (0)	20.7% (6)
Having a normal period	26.7% (4)	14.3% (2)	20.7% (6)
Headache	26.7% (4)	7.1% (1)	17.2% (5)
Being thirsty	26.7% (4)	7.1% (1)	17.2% (5)
Having a short or very light period	13.3% (2)	7.1% (1)	10.3% (3)
Common cold	13.3% (2)	7.1% (1)	10.3% (3)
Stomach bloating	13.3% (2)	0.0% (0)	6.9% (2)
Stomach pain	13.3% (2)	0.0% (0)	6.9% (2)

## How has this trial helped patients and researchers?

The information described above helped the researchers learn more about how LIK066 affects hormones and proteins in women who have PCOS. The changes in hormone levels were too small for researchers to conclude that LIK066 caused the changes. But, the results overall show that this type of treatment might help patients with PCOS. The results from many trials are needed to find out which treatments can be used for patients with PCOS.

The results presented here are for a single trial. This summary shows only the main results from this one trial in a small number of participants. These participants were also treated with LIK066 for a short time. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

## 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 ([www.novctrd.com](http://www.novctrd.com)). Once on the site, click **“Clinical trial results and trial summary for patients”** at the top right of the page. After accepting the terms, go to the bottom left of the page and click **“Search by study number”**. Type **“CLIK066X2205”** into the keyword search box and click **“Search”**.

If you 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 website listed below:

- [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Once you are on the website, type **“CLIK066X2205”** into the **“Other terms”** search box and click **“Search”**.

If more clinical trials are planned, they will be listed on the above public website or [www.novartisclinicaltrials.com](http://www.novartisclinicaltrials.com). Search for **“LIK066”**.

**Full trial title:** A randomized, subject- and investigator-blinded, placebo-controlled pharmacodynamic study of oral LIK066 in overweight and obese women with polycystic ovary syndrome

## Thank you!

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



The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation.

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