Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: LIK066

Protocol Number: CLIK066B2203

Thank you!

Thank you for taking part in the clinical trial for the drug LIK066. You and all of the participants helped researchers learn more about how dietary changes could help participants taking LIK066.

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your 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?

You were in the trial for about 2 months. The trial started in June 2017 and ended in September 2017.

The trial included 54 participants in the United States. This trial had 2 parts. There were 30 participants in Part A and 24 participants in Part B. 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?

Obesity can cause conditions like diabetes, high blood pressure, high cholesterol, and heart disease. Researchers are looking for a better way to help people with obesity lose extra weight and lower the chances that these conditions will happen. Before a drug can be approved for patients to take, researchers do clinical trials to find out how well it works and how safe it is.

LIK066 has been studied in other trials as a possible medicine that may help people with obesity lose weight. The participants in those trials often had diarrhea when taking LIK066. This means they had loose, watery stools. In this trial, the researchers wanted to find a way to lessen diarrhea in a small number of participants who were overweight or had obesity and who were taking LIK066.

In the stomach and small intestine, carbohydrates are broken down into sugars. LIK066 lessens the body's ability to take up sugar from the gut and helps the body remove blood sugar from the kidneys. Researchers think that in participants taking LIK066, the extra sugar that is not absorbed by these organs causes diarrhea.

The researchers in this trial wanted to learn if the participants would have less diarrhea while taking LIK066 if they had fewer carbohydrates in their diet, or if they took a supplement. The researchers also wanted to find out if participants had any medical problems during the trial.

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

- Did reducing carbohydrates in a breakfast lessen the participants' diarrhea?
- Did taking supplements lessen the participants' diarrhea?
- Did the participants' stools change if the participants had different amounts of carbohydrates in a breakfast or if they took a supplement?
- What medical problems did the participants have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women who were overweight or had obesity. The participants in this trial were 21 to 63 years old.

This was an “open-label” trial. This means each participant knew they were taking LIK066, what meal they were eating, and whether or not they got a supplement. The trial staff and sponsor staff also knew what each participant was taking.

This trial was done in 2 parts, with 3 treatment periods in each part. Part A started just before Part B. None of the participants in Part B had been in Part A. In each treatment period, each participant took 1 of 3 treatments. By the end of the trial, each participant had taken all 3 treatments in that part.

There were 5 days between each treatment period. The researchers did this to make sure none of the treatments affected each other.

The figure below shows how the treatment periods were designed.

A computer program was used to randomly choose the order of treatment each participant received. This helped make sure that comparing the results of each treatment was done as fairly as possible.

What happened during the trial?

Before the treatment started in both parts, the trial doctors did tests to make sure the participants could take part in the trial.

The participants began their stay at the trial site 3 days before treatment started. During this time, all the participants ate breakfasts with 50% carbohydrates. The participants gave stool and urine samples.

During each treatment period, each participant took LIK066 in pill form once a day before breakfast. The dose of LIK066 was measured in milligrams, also called mg. All participants took 50 mg of LIK066 for 3 days.

In Part A, there were 30 participants who took all 3 of these treatments. The order was different for each participant:

- a single dose of LIK066 before a breakfast with 50% carbohydrates
- a single dose of LIK066 before a breakfast with 25% carbohydrates
- a single dose of LIK066 before a breakfast with 0% carbohydrates

In Part A, there were 6 participants who were accidentally given a breakfast with 8% carbohydrates instead of 0% carbohydrates. These participants were not included in some of the results.

In Part B, there were 24 participants who took all 3 of these treatments. The order was different for each participant. They took each of these different treatments before a breakfast with 50% carbohydrates:

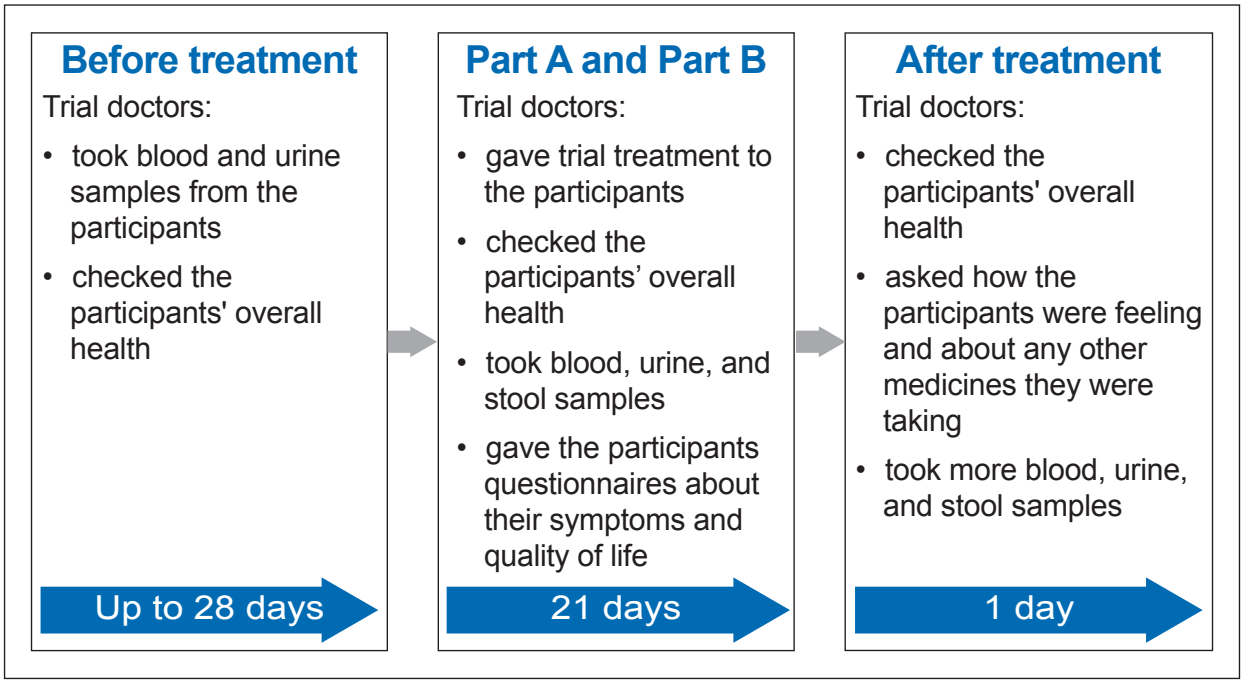
- a single dose of LIK066 only
- a single dose of LIK066 and a supplement called psyllium, which is a fiber
- a single dose of LIK066 and a supplement called calcium carbonate

Calcium carbonate is used as an antacid to treat heartburn, acid indigestion, and upset stomach.

After the treatment ended in both parts, the participants left the trial site.

The trial doctors called the participants 30 days after they left the trial site to check if they were having any serious medical problems.

The chart below shows how the trial was done.



What were the results of the 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 work best and are safest. Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

The researchers did not include the 6 participants in Part A who got the wrong breakfast in the results below.

Did reducing carbohydrates in a breakfast lessen the participants' diarrhea?

Yes. When the participants ate less carbohydrates after taking LIK066, they had less diarrhea.

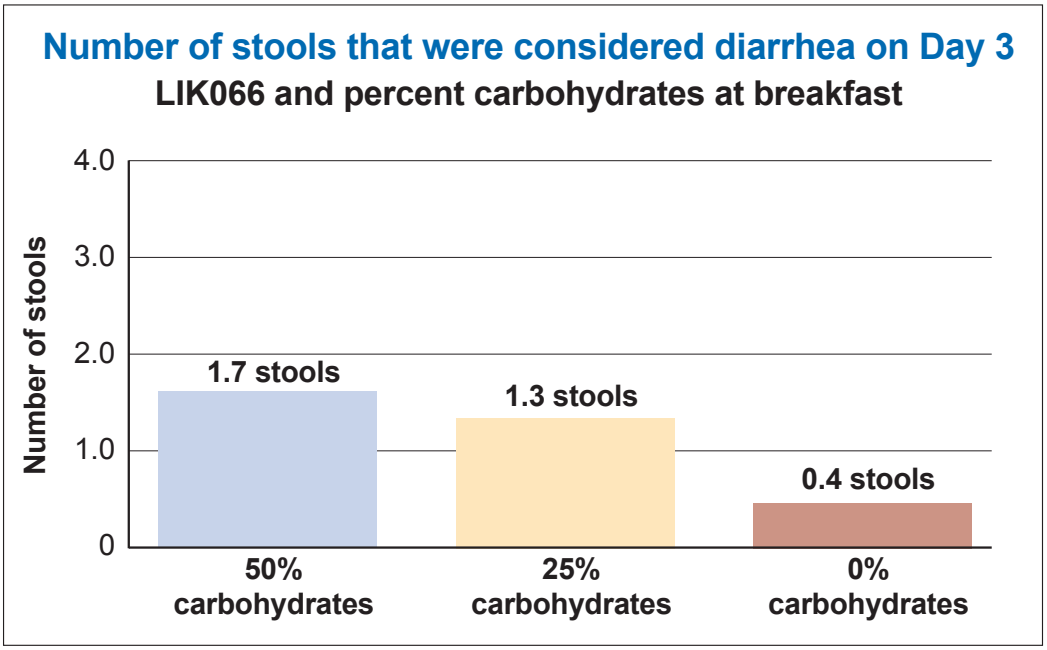
The researchers wanted to know if the participants who ate less carbohydrates had less diarrhea on Day 3 of treatment. This was a main question they wanted to answer.

The trial doctors gave the participants LIK066 right before a breakfast with different amounts of carbohydrates for 3 days. The participants ate a breakfast that was either 50%, 25%, or 0% carbohydrates.

Then, the trial doctors collected and scored the participants' stool samples using the Bristol Stool Chart, also called the BSC. The BSC scores ranged from 1 to 7. A low score meant the stools were hard and were difficult to pass. A high score of a 6 or 7 was considered diarrhea. The trial doctors counted how many stools had a BSC score of 6 or 7 on each day.

Overall, the researchers found that the lower the carbohydrates in the breakfast, the lower the number of stools with a BSC score of 6 or 7.

The chart below shows the number of times participants had diarrhea on Day 3 as defined by stools with a BSC score of 6 or 7. The participants' stools were scored on Day 3 while they took LIK066 and ate breakfasts with different amounts of carbohydrates.



The researchers also kept track of how many stools had a BSC score of 6 or 7 for each participant for all 3 days.

Overall, the researchers found that the results during 3 days of treatment were similar to the results on Day 3. The lower the amount of carbohydrates in the breakfast, the lower the number of stools with a BSC score of 6 or 7.

Did taking supplements lessen the participants' diarrhea?

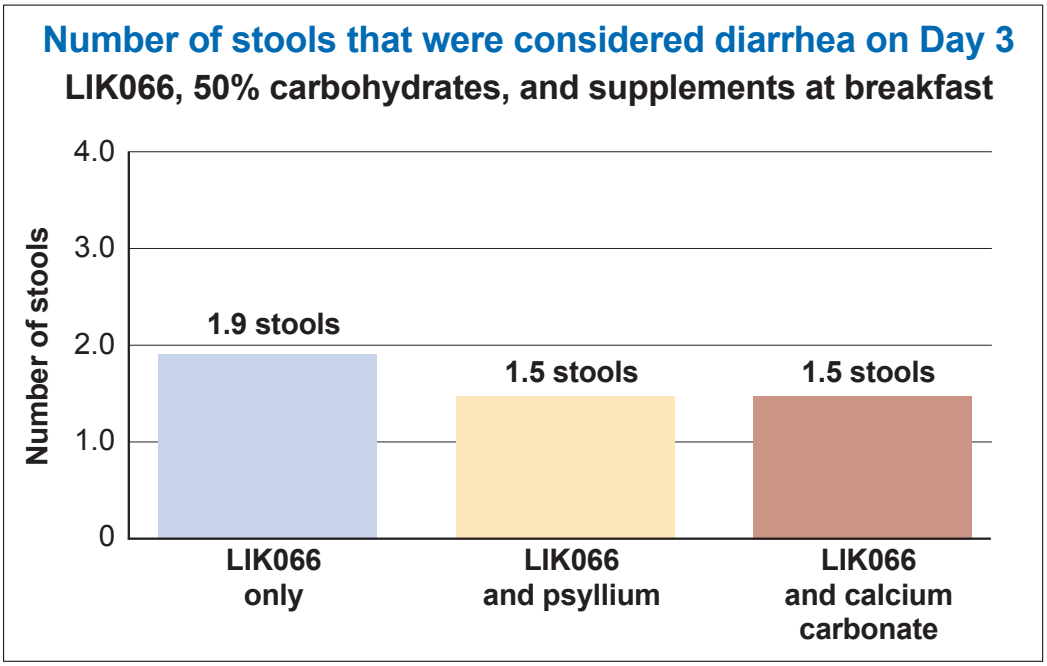
No. Overall, taking supplements with LIK066 did not lessen the participants' diarrhea.

The researchers wanted to know if taking supplements with LIK066 meant the participants would have less diarrhea on Day 3 of treatment. This was a main question they wanted to answer.

The trial doctors gave the participants a breakfast with 50% carbohydrates. Before eating, participants took either LIK066 alone, LIK066 and psyllium, or LIK066 and calcium carbonate for 3 days. Then, the trial doctors collected and scored the participants' stool samples using the BSC.

Overall, the researchers found that there were no differences between the treatment groups in how often the participants had diarrhea when taking LIK066 with supplements. So, taking the supplements did not affect the number of times a participant had diarrhea.

The chart below shows the number of times participants had diarrhea on Day 3 as defined by stools with a BSC score of 6 or 7. The participants' stools were scored on Day 3 while they took LIK066 and a supplement before a breakfast with 50% carbohydrates.



The researchers also kept track of how many stools had a BSC score of 6 or 7 for each participant for all 3 days.

Overall, the researchers found that the results during 3 days of treatment were similar to the results on Day 3. The researchers found that the supplements did not affect the number of times a participant had diarrhea during 3 days of treatment.

Did the participants' stools change if the participants had different amounts of carbohydrates in a breakfast or if they took a supplement?

The researchers measured the following stool characteristics in Part A and Part B of the trial:

- acidity
- weight
- BSC score

Overall, researchers learned that the acidity and weight of participants' stool did not change while taking LIK066:

- with a breakfast with less carbohydrates
- with the supplements psyllium or calcium carbonate

But, the researchers did find that participants who ate a breakfast with 0% carbohydrates had lower BSC scores on Day 3 compared to those who ate a breakfast with 25% or 50% carbohydrates. A lower BSC score meant less watery stool.

What medical problems did the participants have?

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, or the participant needs 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.

This section is a summary of the adverse events that happened during this trial. The results also include the 6 participants in Part A who got the wrong breakfast with 8% carbohydrates and took LIK066.

How many participants had adverse events?

Most of the participants in both parts of the trial had adverse events.

The tables below show how many participants had adverse events during both parts of this trial. The table for Part A includes the 6 participants who were given the wrong breakfast.

Adverse events during Part A of this trial

	LIK066 and 50% carbohydrates (Out of 24 participants)	LIK066 and 25% carbohydrates (Out of 24 participants)	LIK066 and 0% carbohydrates (Out of 24 participants)	LIK066 and 8% carbohydrates (Out of 6 participants)	Total (Out of 30 participants)
How many participants in this trial had adverse events?	87.5% (21)	79.2% (19)	79.2% (19)	83.3% (5)	93.3% (28)

Adverse events during Part B of this trial

	LIK066 only (Out of 24 participants)	LIK066 and psyllium (Out of 24 participants)	LIK066 and calcium carbonate (Out of 24 participants)	Total (Out of 24 participants)
How many participants in this trial had adverse events?	87.5% (21)	79.2% (19)	91.7% (22)	10.0% (24)

In both parts of the trial, none of the participants stopped taking the trial drug due to adverse events.

What were the most common serious adverse events?

None of the participants in this trial had a serious adverse event. None of the participants died during this trial.

What were the most common adverse events?

Diarrhea was the most common adverse event during Part A of this trial. This happened in 83.3% of participants, which was 25 out of 30 participants. The adverse events below happened in at least 2 participants. There were other adverse events, but these happened in fewer participants. The table for Part A includes the 6 participants who were given the wrong breakfast.

Adverse events that happened during Part A of this trial

Adverse event	LIK066 and 50% carbohydrates (Out of 24 participants)	LIK066 and 25% carbohydrates (Out of 24 participants)	LIK066 and 0% carbohydrates (Out of 24 participants)	LIK066 and 8% carbohydrates (Out of 6 participants)	Total (Out of 30 participants)
Diarrhea	83.3% (20)	70.8% (17)	58.3% (14)	50.0% (3)	83.3% (25)
Constipation	25.0% (6)	4.2% (1)	20.8% (5)	16.7% (1)	33.3% (10)
Bloating	4.2% (1)	4.2% (1)	12.5% (3)	16.7% (1)	20.0% (6)
Passing gas	4.2% (1)	0.0% (0)	0.0% (0)	33.3% (2)	10.0% (3)
Stomach pain	4.2% (1)	0.0% (0)	4.2% (1)	0.0% (0)	6.7% (2)
Redness of the skin	0.0% (0)	4.2% (1)	4.2% (1)	0.0% (0)	6.7% (2)
Nausea	4.2% (1)	0.0% (0)	4.2% (1)	0.0% (0)	6.7% (2)

Diarrhea was also the most common adverse event during Part B of this trial. This happened in 100.0% of participants, which was 24 out of 24 participants. The adverse events below happened in at least 2 participants. There were other adverse events, but these happened in fewer participants.

Adverse events that happened during Part B of this trial

Adverse event	LIK066 only (Out of 24 participants)	LIK066 and psyllium (Out of 24 participants)	LIK066 and calcium carbonate (Out of 24 participants)	Total (Out of 24 participants)
Diarrhea	83.3% (20)	70.8% (17)	91.7% (22)	100.0% (24)
Passing gas	8.3% (2)	8.3% (2)	16.7% (4)	20.8% (5)
Headache	8.3% (2)	4.2% (1)	12.5% (3)	20.8% (5)
Stomach pain	8.3% (2)	4.2% (1)	8.3% (2)	16.7% (4)
Indigestion	0.0% (0)	8.3% (2)	4.2% (1)	12.5% (3)
Nausea	0.0% (0)	4.2% (1)	12.5% (3)	12.5% (3)
Constipation	0.0% (0)	8.3% (2)	4.2% (1)	8.3% (2)

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

How has this trial helped patients and researchers?

The information described above helped the researchers better understand how to lessen diarrhea in people who take LIK066.

The results presented here are for a single trial. Researchers look at the results of many trials to decide which treatments work best and are safest. This summary shows only the main results from this one trial in a small number of participants. 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). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CLIK066B2203"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial staff at your trial site.

You can find more information about this trial on the website listed below:

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03198767"** into the search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"LIK066"**.

Full trial title: A randomized, open label, two-part, three-period, cross-over study to investigate the effects of carbohydrate in diet and to evaluate supplements on the gastrointestinal tolerability of LIK066 in overweight or obese subjects

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

CISCRP

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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