NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of TMT212 on combination birth control in women with cancer

Protocol number: CTMT212X2102

Our thanks to the participants!

Novartis, the sponsor of this clinical trial, would like to thank the participants who took part in this trial for the drug TMT212, also known as trametinib. They helped researchers learn more about the effects of TMT212 on combination birth control in people with cancer.

Clinical trial participants belong to a large community of people around the world. Their invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare.

Why was the research needed?

Researchers want to learn if some cancer drugs affect how well **combination birth control** works to prevent pregnancy. Combination birth control is a commonly prescribed type of birth control pill that contains both progestin and estrogen to prevent pregnancy. Progestin and estrogen are female hormones.

TMT212 is a drug that is approved to treat certain types of cancer, such as some types of melanoma, non-small cell lung cancer, and some types of thyroid cancer.

Researchers designed this trial to learn if the cancer drug TMT212 could cause women's bodies to break down birth control hormones faster. This could change the amount of birth control hormones in the blood, and how well they work to prevent pregnancy.

In this trial, researchers compared the levels of birth control hormones in women's blood before and after they took TMT212.

Trial treatments

The drugs taken in this trial were:

TMT212, also known as trametinib, taken by mouth as a pill

Combination birth control, taken by mouth as a pill. It contained a type of progestin called **norethindrone (NE),** and a type of estrogen called **ethinyl estradiol (EE).**

Trial purpose

This trial was done to learn more about the effects of TMT212 on the levels of NE and EE in the blood. The main questions the researchers wanted to answer in this trial were:

- Did TMT212 affect the levels of birth control hormones in the participants' blood?
- What medical problems did the participants have during the trial?

How long was this trial?

This trial was designed so that an individual participant could take part for at least 2 months. The participants began on different dates. The trial started in October 2016 and ended in August 2019.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

19 women were in this trial. Each participant in this trial had stage 3 or 4 cancer that:

- Had no approved treatment
- Other approved cancer drugs did not work to treat their cancer
- Trial doctors thought TMT212 may work to treat their cancer
- Trial doctors thought a combination birth control would not worsen

Participants' ages ranged from 34 to 59 years. They were 47 years old on average.

Participants took part at 5 trial sites in these countries:

- Belgium – 3 participants
- The Netherlands – 3 participants
- Spain – 1 participant
- The United Kingdom – 11 participants
- The United States – 1 participant

What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment each participant took. In this trial, all participants took combination birth control and TMT212.

What happened during this trial?

During screening

Up to 30 days before taking the trial treatment, trial doctors checked participants' cancer and general health to make sure they could be in this clinical trial. 19 participants could take part in this trial.

During treatment

The participants took both:

- **Combination birth control,** taken as a pill one time a day from trial Day 1 to 21. It contained 1 milligram (mg) NE and 0.035 mg EE.
- **TMT212**, 2 mg taken as a pill one time a day from trial Day 6 to 21

After trial Day 21, participants could continue to take combination birth control or TMT212 if they wanted to and the trial doctor agreed it could help.

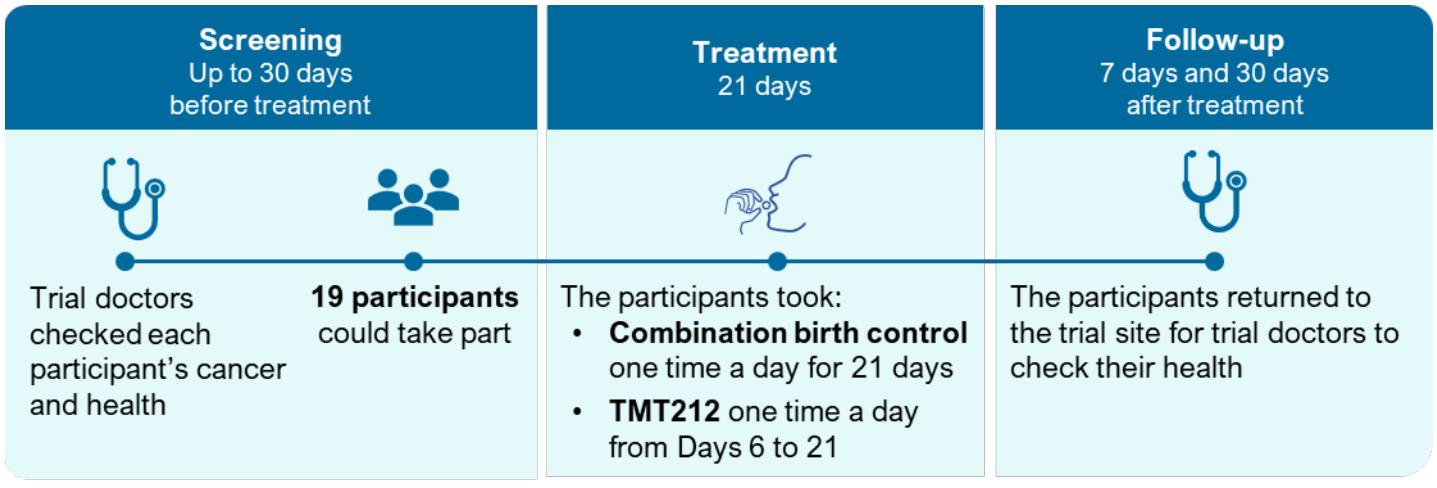
In addition to the 2 trial drugs above, participants could take certain other cancer treatments.

Researchers checked the participants' cancer and general health throughout the trial.

During follow-up

Participants returned to their trial site for follow-up visits 7 days and 30 days after taking their last dose of TMT212.

How researchers designed this trial:



What were the main results of this trial?

This is a summary of the overall results for all participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

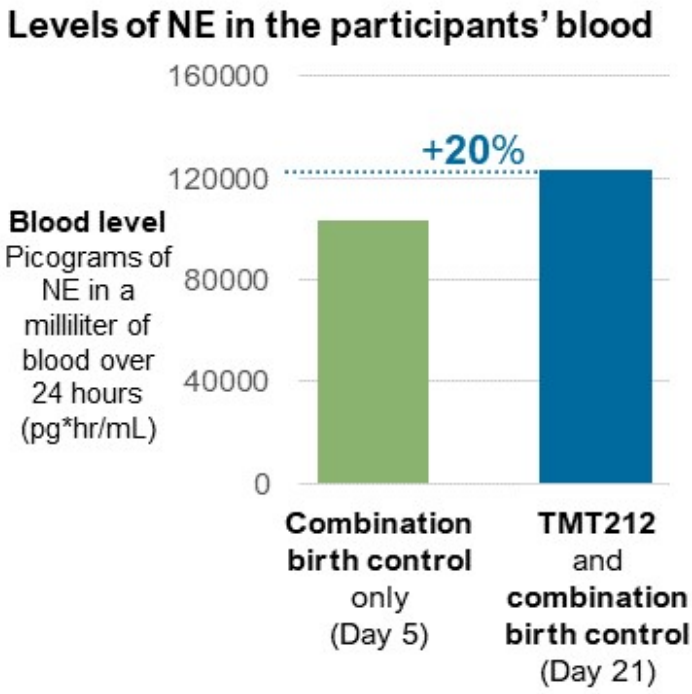
Did TMT212 affect the levels of birth control hormones in the participants' blood?

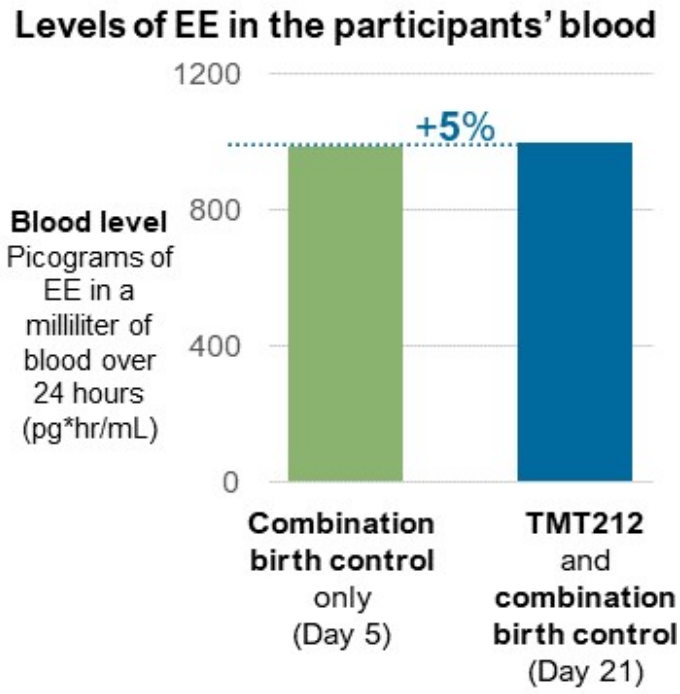
To find this out, the researchers measured the levels of NE and EE birth control hormones in participants' blood. They compared the overall levels before the participants took TMT212 to after.

The participants gave blood samples on:

- Day 5 after taking combination birth control only
- Day 21 after taking both combination birth control and TMT212

On average, TMT212 slightly raised the level of NE in the participants' blood. The level of EE stayed about the same. The clinical trial team concluded that TMT212 did not affect how well the birth control worked.





What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is an 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 an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during the treatment period and during the 30 days after each participant’s last dose of trial treatment. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the serious adverse events?

During this trial, 8 participants had at least one serious adverse event. All of the serious adverse events that happened during this trial are listed in the table below.

	Percent % (out of 19 participants)
Buildup of fluid in the belly Ascites	**11%** (2)
Bowels stops working Ileus	**5%** (1)
Feeling sick to the stomach Nausea	**5%** (1)
Lung infection Pneumonia	**5%** (1)
Low blood sugar Hypoglycemia	**5%** (1)
Muscle inflammation Myositis	**5%** (1)
Cancer that spreads to the intestines Intestinal metastasis	**5%** (1)

During this clinical trial, 4 participants died within 30 days of taking trial treatment. The investigators believe the deaths were related to the participants’ cancer.

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 20% (4 out of 19) of participants are listed in the table below.

Most common non-serious adverse events

	Percent % (out of 19 participants)
Rash	**53%** (10)
Feeling sick to the stomach Nausea	**37%** (7)
Diarrhea	**32%** (6)
Throwing up Vomiting	**26%** (5)
Low levels of red blood cell Anemia	**21%** (4)
Possible sign of illness or infection Blood alkaline phosphatase increased	**21%** (4)
Sore mouth Stomatitis	**21%** (4)

How has this trial helped?

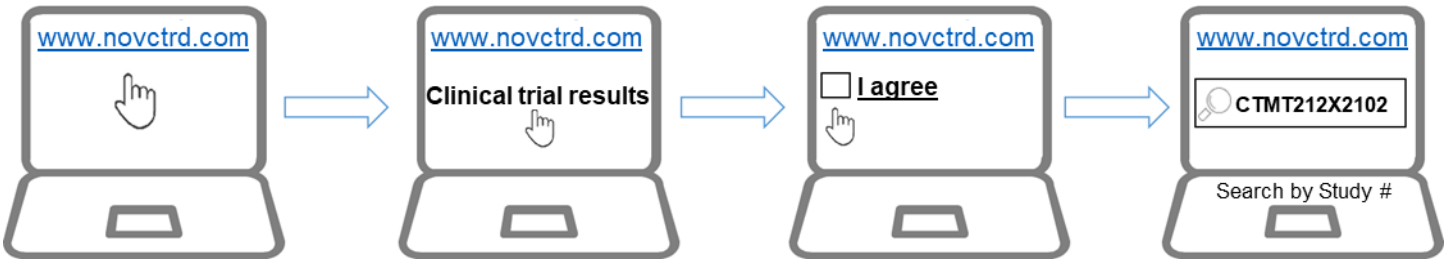
This trial helped researchers learn about how TMT212 affects the levels of birth control hormones in women with cancer. The results support the use of combination birth control in women who take TMT212 to treat cancer.

There were no safety concerns for TMT212. The safety results in this trial were similar to what is known for the approved drug, TMT212.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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).



You can find more information about this trial on this website:

- www.clinicaltrials.gov. Use the NCT identifier NCT02705963 in the search field.

Full clinical trial title: A Phase I, open-label study to determine the effect of repeat dosing of trametinib on the pharmacokinetics of a combined oral contraceptive (norethindrone plus ethinyl estradiol) in female patients with solid tumors

Thank you

We thank the participants for taking part in this trial. Clinical trial participants belong to a large community of participants around the world. The participants helped researchers answer important health questions and test new medical treatments.

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

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