

Summary of Clinical Trial Results

A study of cobimetinib with niraparib, with or without atezolizumab, in women with ovarian cancer

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- Women who took part in the study and
- Members of the public.

This summary is based on information known at the time of writing (November 2023).

The study started in December 2018 and ended in July 2023. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from those seen in other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

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Thank you to the women who took part in this study

The women who took part have helped researchers to answer important questions about ovarian cancer and the medicines studied – 'cobimetinib', 'niraparib' and 'atezolizumab'.

Key information about this study

- This study was done to find out if a combination of cancer medicines, cobimetinib and niraparib, taken with or without another medicine called atezolizumab, could make ovarian cancer tumours smaller or completely disappear, and was safe to take.
- During the study, women with ovarian cancer were selected by chance to get one of two treatment combinations, as shown here.

Combination 1:
Cobimetinib
plus niraparib

Combination 2:
Cobimetinib
plus niraparib
plus atezolizumab

- This study included 76 women in three countries.
- The main findings were that:
 - The ovarian cancer tumours got smaller or completely disappeared in 35% of women (13 out of 37 women) who took cobimetinib and niraparib.



- The ovarian cancer tumours got smaller or completely disappeared in 27% of women (10 out of 37 women) who took cobimetinib, niraparib and atezolizumab.



- Around 21% of women (8 out of 39 women) taking cobimetinib and niraparib and 24% of women (9 out of 37 women) taking cobimetinib, niraparib and atezolizumab had serious side effects.
- At the time of writing this summary, the study had ended.

1. General information about this study

Why was this study done?

This study was done to learn more about how best to treat women with ovarian cancer. Ovarian cancer can be grouped into different types, with the most common being 'epithelial ovarian cancer', a type of cancer that starts in the cells that cover the ovaries. Two other types of cancer – 'fallopian tube cancer' and 'primary peritoneal cancer' – are similar to ovarian cancer and are treated the same way. Fallopian tube cancer starts in the fallopian tubes, which connect the ovaries to the womb (uterus). Primary peritoneal cancer is related to ovarian cancer and starts in the peritoneum, a thin layer of tissue that lines the abdomen and covers some of the organs. This study included women with any of the above three cancer types.

Women with ovarian cancer are typically treated with surgery and a type of medicine that kills cancer cells, called chemotherapy. The latter type of treatment uses two different types of chemotherapy drugs, including one that uses platinum to kill cancer cells (called 'platinum-based chemotherapy'), to reduce or prevent cancer cell growth. However, chemotherapy may work only for a limited time, meaning that the cancer may return or start to grow again. Because of this, women with ovarian cancer need new medicines to aim to reduce the size of their tumours. People may be able to manage their cancer better if their tumours are smaller.

In this study, researchers tested a new way of trying to treat women with ovarian cancer that had spread or come back at least 6 months after treatment. These women had taken platinum-based chemotherapy, but the treatment was no longer making their tumours smaller. Researchers wanted to see if taking a combination of medicines, 'cobimetinib' with 'niraparib', taken with or without 'atezolizumab', could reduce the size of tumours. Cobimetinib works by blocking signals that cancer cells use to grow and divide. Niraparib blocks a protein called poly(ADP-ribose) polymerase (also known as PARP), which is involved in repairing breaks in DNA. Atezolizumab is a type of 'immunotherapy' that encourages the body's own immune system to attack cancer cells. Scientists think that combining these medicines may make tumours smaller than if the medicines were used on their own. The study also looked at whether these new combinations were safe, that is whether they caused any new side effects or any more side effects than previous treatments.

What were the medicines being studied?

This study looked at two combinations of medicines:

- Cobimetinib taken together with niraparib
- Cobimetinib taken together with niraparib and atezolizumab

These medicine combinations are new – they are not existing treatments for ovarian cancer.

Cobimetinib (known by its brand name, COTELLIC®) is one of the medicines that were studied here.

- You say this as 'coh – bee – met – in – ib'.
- This is a type of cancer medicine that blocks the signals that cancer cells use to grow and divide.
- When people take cobimetinib, their tumours may get smaller.

Niraparib (known by its brand name, Zejula®) is another one of the medicines that were studied here.

- You say this as ‘nir – rap – ar – ib’.
- This is a type of cancer medicine that blocks a protein called PARP, which is involved in repairing breaks in DNA.
- When people take niraparib, their tumours may get smaller.

Atezolizumab (known by its brand name, TECENTRIQ®) is another one of the medicines that were studied here.

- You say this as ‘a – teh – zo – liz – oo – mab’.
- This is a type of cancer medicine that is used to encourage the body’s immune system to attack tumours. This type of treatment is called ‘immunotherapy’.
- The body’s immune system fights diseases like cancer. However, cancer cells can block the immune system from attacking the cancer. Atezolizumab releases this block – meaning that the immune system is able to fight the cancer cells.
- When people take atezolizumab, their tumours may get smaller.

What did researchers want to find out?

- Researchers did this study to see how well cobimetinib worked when taken together with niraparib, with or without atezolizumab, in women with ovarian cancer (see section 4, “What were the results of the study?”).
- They also wanted to find out how safe the two medicine combinations were, by checking how many women had side effects and seeing how serious they were, when taking these medications during this study (see section 5, “What were the side effects?”).

The main questions that researchers wanted to answer were:

1. Can taking cobimetinib in combination with niraparib, taken with or without atezolizumab, make the tumours of women with ovarian cancer smaller or disappear completely?
2. How many women taking cobimetinib in combination with niraparib, taken with or without atezolizumab, experienced side effects caused by the treatments – and how serious were the side effects?

What kind of study was this?

This study was a ‘Phase 1’ study, which means that this was one of the first studies for cobimetinib taken together with niraparib, with or without atezolizumab. A small number of women with ovarian cancer took cobimetinib with niraparib, with or without atezolizumab, and the researchers did medical tests on the women who took part to find out more about how well these medicines worked and how safe they were.

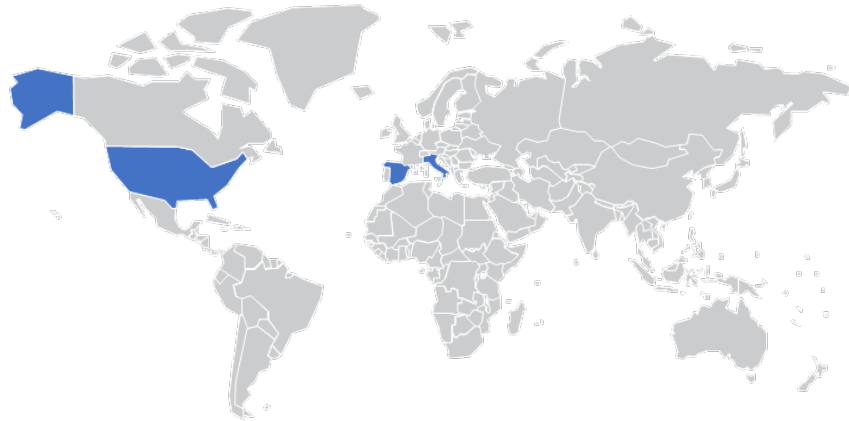
The study was done in two stages. Stage 1 was designed to assess safety. In stage 2, it was decided by chance which of the two combinations women in the study would be given. Deciding by chance which group people will be in makes it more likely that the types of people in both groups will be a similar mix (for example, similar ages). Other than the different medicines given in each group, all other care was the same.

When and where did the study take place?

The study started in December 2018 and ended in July 2023. This summary was written after the study had ended.

The study took place at 17 study centres – across three countries in North America and Europe. The following map shows the countries where this study took place.

- United States
- Spain
- Italy



2. Who took part in this study?

In this study, 76 women with ovarian cancer took part.

Women who took part in the study were between 44 and 81 years of age. In this study, 71 out of the 76 women were White, one woman was Black, and the race of four women was unknown.

Women could take part in the study if:

- They had been treated before with a type of medicine that kills cancer cells using platinum – called ‘platinum-based chemotherapy’ – for ovarian cancer
- Their cancer had spread after at least 6 months of treatment with the ‘platinum-based chemotherapy’
- They could perform activities as well or almost as well as they could before the illness

Women could not take part in the study if:

- They were previously treated with a medicine that blocks the same signals that cancer cells use to grow and divide as those blocked by cobimetinib, a medicine that blocks DNA repair like niraparib, or a medicine that helps the immune system fight cancer cells (like atezolizumab)

3. What happened during the study?

During the study, women were assigned by chance to get one of two treatment combinations. The choice of treatment combination was selected by a computer at random. Women got either:

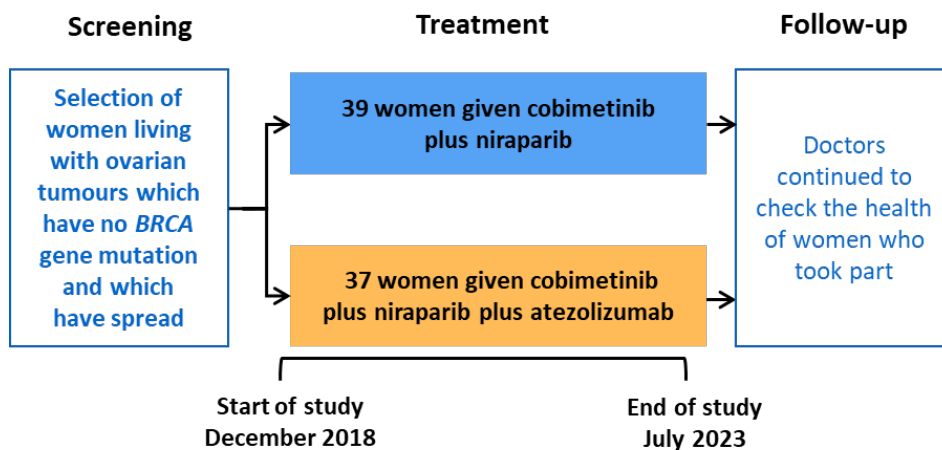
- Combination 1: Cobimetinib plus niraparib
- Combination 2: Cobimetinib plus niraparib plus atezolizumab

The medicines in this study were given in ‘treatment cycles’. Each treatment cycle lasted 4 weeks.

This table shows the number of women who took each study treatment, and how often the medicines were taken.

	Cobimetinib plus niraparib	Cobimetinib plus niraparib plus atezolizumab
Number of women in each group	39	37
How the medicines were taken	Cobimetinib: 60 mg tablets by mouth Niraparib: 200 mg tablets by mouth	Cobimetinib: 60 mg tablets by mouth Niraparib: 200 mg tablets by mouth Atezolizumab: 840 mg injected into the vein
When and how often the medicines were taken in the treatment cycle (each treatment cycle was 4 weeks)	Cobimetinib: once a day on Days 1 to 21 Niraparib: once a day on Days 1 to 28	Cobimetinib: once a day on Days 1 to 21 Niraparib: once a day on Days 1 to 28 Atezolizumab: once a day on Day 1 and Day 15

This picture shows what happened in the study for each of the two groups. When the study finished, the women who took part were asked to go back to their study centre for more visits – to check their overall health.



4. What were the results of the study?

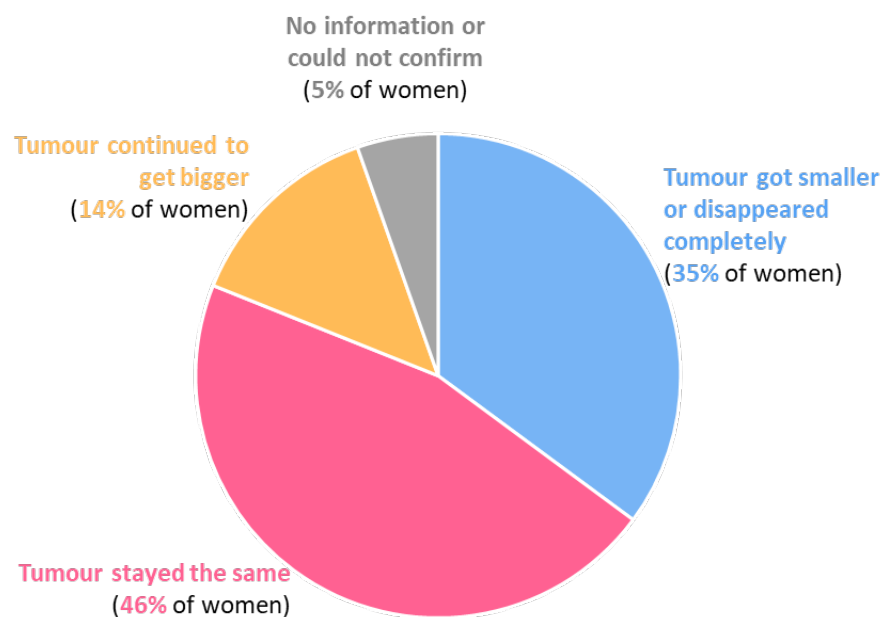
This information was collected from December 2018 to July 2023.

Question 1: Can taking cobimetinib in combination with niraparib, taken with or without atezolizumab, make the tumours of women with ovarian cancer smaller or disappear completely?

Researchers looked at what had happened to the tumours of women who took **combination 1**: cobimetinib and niraparib – or **combination 2**: cobimetinib, niraparib and atezolizumab. Women who had a genetic change in their cells, called a mutation in the *BRCA* gene, were not included in this analysis (2 out of 76 women; both were in the **combination 1** group). Therefore, the results are based on 37 women (out of 39) who took cobimetinib and niraparib and 37 women who took cobimetinib, niraparib and atezolizumab.

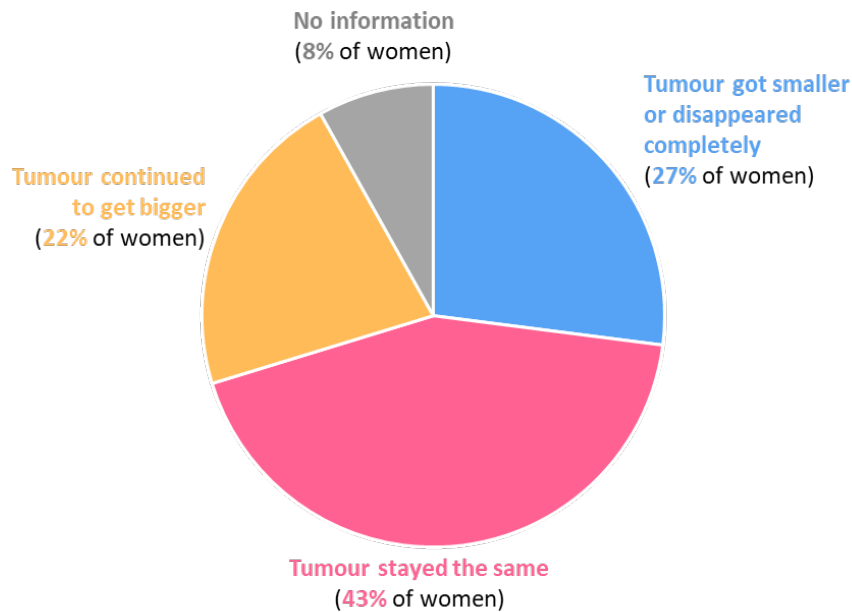
How well did the combination of cobimetinib and niraparib work at making the tumours smaller or disappear completely?

- The tumours got smaller or disappeared completely in 35% of women (13 out of 37 women) who took cobimetinib and niraparib.



How well did the combination of cobimetinib, niraparib and atezolizumab work at making the tumours smaller or disappear completely?

- The tumour got smaller or disappeared completely in 27% of women (10 out of 37 women) who took cobimetinib, niraparib and atezolizumab.



Question 2: How many women taking cobimetinib in combination with niraparib, taken with or without atezolizumab, experienced side effects caused by the treatments – and how serious were the side effects?

Another piece of information that researchers collected was the side effects women experienced with cobimetinib and niraparib, with or without atezolizumab.

- See section 5 for a summary of side effects.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the women in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

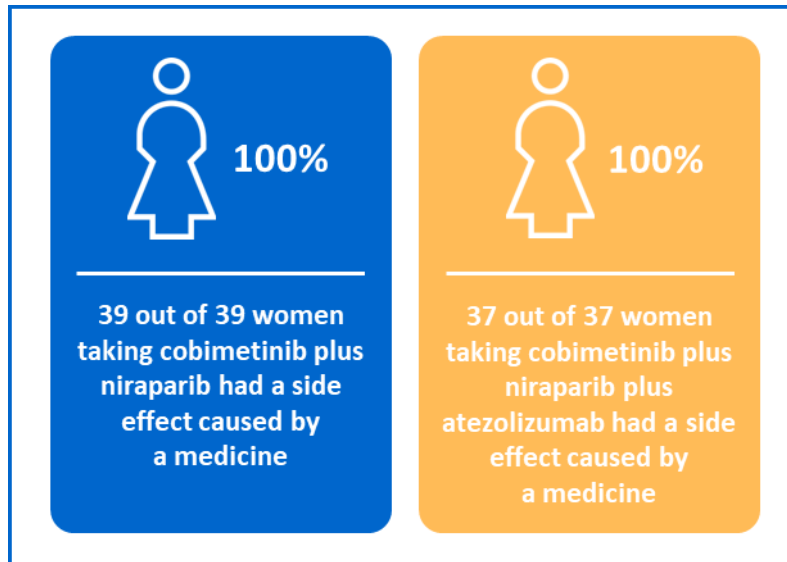
A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, 22% of women (17 out of 76 women) had at least one serious side effect.

- Around 21% of women (8 out of 39 women) taking cobimetinib plus niraparib had a serious side effect.
- Around 24% of women (9 out of 37 women) taking cobimetinib plus niraparib plus atezolizumab had a serious side effect.

Most common side effects

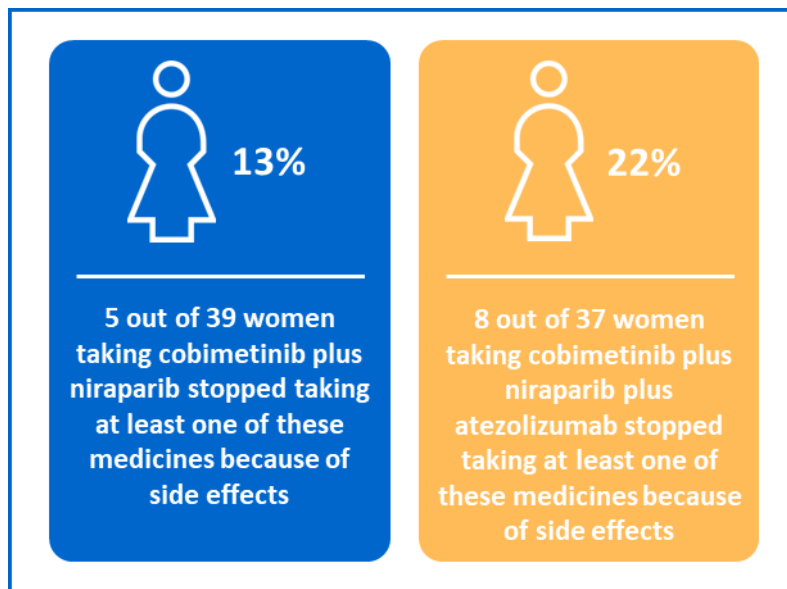
During this study, all women had at least one side effect (serious or not). This picture shows the number of women in each group who had side effects caused by the medicines taken.



The most common side effects caused by the medicines taken are shown in the following table – these are the top 10 most common side effects across both treatment groups. Some women had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	Women taking cobimetinib plus niraparib (39 women total)	Women taking cobimetinib plus niraparib plus atezolizumab (37 women total)
Feeling sick (nausea)	72% (28 out of 39 women)	84% (31 out of 37 women)
Frequent, loose, watery stools (diarrhoea)	74% (29 out of 39 women)	73% (27 out of 37 women)
Throwing up (vomiting)	72% (28 out of 39 women)	51% (19 out of 37 women)
Liver damage – shown by higher levels of something called ‘AST’ in the blood	46% (18 out of 39 women)	35% (13 out of 37 women)
Low level of red blood cells	46% (18 out of 39 women)	32% (12 out of 37 women)
Low energy levels	36% (14 out of 39 women)	43% (16 out of 37 women)
Feeling tired	33% (13 out of 39 women)	46% (17 out of 37 women)
Rash	36% (14 out of 39 women)	32% (12 out of 37 women)
Muscle damage – shown by higher levels of something called ‘creatinine phosphokinase’ in the blood	39% (15 out of 39 women)	27% (10 out of 37 women)
Lower appetite	26% (10 out of 39 women)	35% (13 out of 37 women)

During the study, some women decided to stop taking their medicine because of side effects. This picture shows the number of women who stopped taking their medicine because of side effects.



No women in this study died because of side effects related to the treatment.

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from one study of 76 women with ovarian cancer that has spread. These results helped researchers learn more about how well the combination of cobimetinib plus niraparib, with or without atezolizumab, worked to treat this type of cancer, and how safe these treatment combinations were.

Overall, this study showed that the combination of cobimetinib plus niraparib, with or without atezolizumab, made the tumours smaller or disappear completely in approximately 3 to 4 out of every 10 women. The women in this study did not have any new side effects that had not been seen before in people who took these medicines in other studies.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from those seen in other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

This is the first study to look at the combination of cobimetinib and niraparib, with or without atezolizumab, in women with ovarian cancer. No other studies looking at this combination are happening at the moment, but they may happen in the future.

Other studies looking at medicines that block the signals that cancer cells use to grow and divide are happening. These studies include women with ovarian cancers or people with other types of cancer.

Other studies looking at the safety and effects of atezolizumab are happening. These studies are looking at the use of atezolizumab in different situations, for example:

- In other types of cancer that affect the female reproductive system.
- In ovarian cancer that has come back after treatment or not responded to other treatment.
- In other types of cancer, including breast and lung cancer.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

- <https://clinicaltrials.gov/ct2/show/results/NCT03695380>
- <https://forpatients.roche.com/en/trials/cancer/oc/a-clinical-study-of-cobimetinib-administered-in-combina-24843.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Primary results and characterization of patients with exceptional outcomes in a phase 1b study combining PARP and MEK inhibition, with or without anti-PD-L1, for *BRCA* wild-type, platinum-sensitive, recurrent ovarian cancer”. The authors of the scientific paper are: David Mutch, Athina Voulgari, Xian (Marissa) Chen, William H. Bradley, Ana Oaknin, and others. The paper is published online ahead of print in the journal ‘Cancer’: Cancer 2024. Jan 30. doi: 10.1002/cncr.35222. Online ahead of print.

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – <https://forpatients.roche.com//en/trials/cancer/oc/a-clinical-study-of-cobimetinib-administered-in-combina-24843.html>
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd, which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Clinical Study of Cobimetinib Administered in Combination With Niraparib, With or Without Atezolizumab to Patients With Advanced Platinum-sensitive Ovarian Cancer”.

- The protocol number for this study is: YO40482.
- The ClinicalTrials.gov identifier for this study is: NCT03695380.