ForPatients
by Roche

Ovarian Cancer

A clinical trial to look at how well cobimetinib works in combination with another drug called niraparib to slow, stop or reverse the course of ovarian cancer, and whether it works better when it is given with or without another drug called atezolizumab.

A Clinical Study of Cobimetinib Administered in Combination With Niraparib, With or Without Atezolizumab to Patients With Advanced Platinum-sensitive Ovarian Cancer

Trial Status	Trial Runs In	Trial Identifier
Completed	3 Countries	NCT03695380 2018-000631-27 YO40482

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase Ib Study of Cobimetinib Administered in Combination With Niraparib, With or Without Atezolizumab, To Patients With Advanced Platinum-sensitive Ovarian Cancer

Trial Summary:

The study will include a safety run-in phase (Stage 1) and a randomization phase (Stage 2). The purpose of Stage 1 is to evaluate the safety of cobimetinib when administered in combination with niraparib (Cohort 1) and cobimetinib with niraparib plus atezolizumab (Cohort 2). Stage 1 will enable patient enrollment in the randomized phase of the study (Stage 2) with both regimens at the recommended dose levels from Stage 1. Stage 2 is a randomized, dose-expansion phase, evaluating clinical outcomes in patients with advanced platinum-sensitive ovarian cancer. All patients will continue to receive study treatment until disease progression (according to "Response Evaluation Criteria in Solid Tumors" (RECIST), Version 1.1, unacceptable toxicity, death, or patient or investigator decision to withdraw, whichever occurs first.

Hoffmann-La Roche	Phase 1
Sponsor	Phase

NCT03695380 2018-000631-27 YO40482
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
Female	# 18 Years	No

How does the YO40482 clinical trial work?

This clinical trial is recruiting people who have advanced ovarian cancer.

The purpose of this clinical trial is to test the safety and effectiveness of cobimetinib when given with another drug called niraparib, and whether it works better when given with or without another drug called atezolizumab.

How do I take part in this clinical trial?
To be able to take part in this clinical trial, you must have been diagnosed with advanced ovarian cancer and have already tried a specific chemotherapy, called platinum chemotherapy, once or twice.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, if you are not currently pregnant but can become pregnant, you will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will i be given if I join this clinical trial?
This clinical trial has two Stages. The doses of cobimetinib and niraparib will be confirmed in Stage 1. If you have the BRCA mutation, you will only be able to enter Stage 1 of this trial. If you do not have the BRCA mutation you may be entered into either Stage 1 or Stage 2.

Everyone who enters Stage 1 of this clinical trial will be split into 2 groups randomly (like flipping a coin) and given, as a starting dose, either:

- cobimetinib (3 tablets to swallow every day for 3 weeks and then not taken for 1 week) and niraparib (2 capsules to swallow every day)
- OR cobimetinib (3 tablets to swallow every day for 3 weeks and then not taken for 1 week) and niraparib (2 capsules to swallow every day) and atezolizumab (drug given into your vein every 2 weeks)

Depending on how patients responded to treatment in Stage 1 the doctors may change the dose of cobimetinib and/or niraparib before Stage 2. After the doses of niraparib and cobimetinib are confirmed in Stage 1, Stage 2 will open. Everyone who enters Stage 2 of this clinical trial will also be split into 2 groups randomly and given the same treatments as those listed for Stage 1.

Whether you join Stage 1 or Stage 2, you will have an equal chance of being placed in either treatment group. Doctors will be monitoring you for and side effects related to the treatment you have been given. In Stage 2, if you are in the group that is not being given atezolizumab and your cancer gets worse, you may be allowed to swap to the group that is being given atezolizumab.

How often will i be seen in follow-up appointments, and for how long?
You will be given the clinical trial treatment for as long as it can help you. You are free to stop this treatment at any time. After being given treatment, you will still be monitored by telephone call or clinic visits every 3 months. This will include checks to see how you are responding to the treatment and any side effects that you may be having.

What happens if i am unable to take part in this clinical trial?
If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT03695380

Trial-identifier: NCT03695380

Inclusion Criteria:

- Ability to comply with the study protocol, in the investigator's judgment
- Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures, including the completion of patient-reported outcome questionnaires
- Histological diagnosis of high-grade serous or Grade 2 or Grade 3 endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Previous treatment with a minimum of one and a maximum of two prior platinum based treatment regimens
- Platinum-sensitive disease

- Availability of tumor biopsy tissue prior to first dose of study treatment with confirmation by the central laboratory that the sample is not only of adequate quality but also assignable to a molecularly defined subgroup based on breast cancer susceptibility gene (BRCA) and loss of heterozygosity (LOH) status
- Measurable disease, as defined by Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1)
- Adequate hematologic and organ function
- Eastern Cooperative Oncology Group Performance Status of 0 or 1
- Life expectancy of at least 12 weeks
- Resolved or stabilized toxicities resulting from previous therapy to Grade 1
- Negative HIV test at screening
- Negative hepatitis B surface antigen and total hepatitis B core antibody (HBcAb) test, or positive total HBcAb test followed by quantitative hepatitis B virus (HBV) DNA < 500 IU/mL test at screening
- Negative hepatitis C virus (HCV) antibody test, or positive HCV antibody test followed by a negative HCV RNA test at screening
- For women of childbearing potential: Women must remain abstinent or use two contraceptive methods with a failure rate of <1% per year during the treatment period and for at least 3 months after the last dose of cobimetinib, 6 months after the last dose of niraparib, and 5 months after the last dose of atezolizumab. Women must refrain from donating eggs during this same period

Exclusion Criteria:

- Prior treatment with mitogen-activated protein kinase inhibitor, polyadenosine diphosphate-ribose polymerase inhibitor, or immune checkpoint inhibitor therapies
- Prior chemotherapy, hormonal therapy, radiotherapy, antibody therapy, or other immunotherapy, gene therapy, vaccine therapy, or treatment with experimental drugs within 14 days prior to first dose of study treatment
- Treatment with systemic immunostimulatory agents within 28 days or 5 half-lives of the drug prior to initiation of study treatment
- Treatment with systemic immunosuppressive medication 14 days prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during the study
- History of other malignancy that could affect compliance with the protocol or interpretation of results, or known to have potentially fatal outcome
- Symptomatic and/or untreated central nervous system metastases
- Surgical procedure, significant traumatic injury within 14 days prior to enrollment, or anticipation of need for major surgical procedure during the study
- Minor surgical procedure within 3 days
- History or evidence of retinal pathology on ophthalmic examination
- Left ventricular ejection fraction below institutional lower limit of normal
- History of clinically significant cardiovascular dysfunction
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on the screening chest computed tomography scan
- History or evidence of inherited bleeding diathesis or significant coagulopathy at risk for bleeding
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins, or to any component of the atezolizumab formulation
- Known allergy or hypersensitivity to any component of the cobimetinib or niraparib formulation
- Active or history of autoimmune disease or immune deficiency including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, anti-phospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain-Barre syndrome, or multiple sclerosis
- Uncontrolled serious medical or psychiatric illness
- History of malabsorption or other condition that would interfere with absorption of oral study drugs, including preexisting duodenal stent or ongoing intestinal obstruction

- Active tuberculosis
- Severe infection within 14 days prior to initiation of study treatment, including, but not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia
- Treatment with therapeutic oral or IV antibiotics within 7 days prior to initiation of study treatment
- Treatment with a live, attenuated influenza vaccine within 28 days prior to study treatment initiation, at any time during the study, and for at least 5 months after the last dose of study drug
- Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the patient at high risk from treatment complications
- Previous treatment with strong CYP3A inhibitors (such as ketoconazole and clarithromycin), strong CYP3A inducers (such as carbamazepine and phenytoin), and moderate CYP3A inducers (such as efavirenz, modafinil) within 7 days prior to the initiation of study treatment or with ongoing requirements for these medications
- Pregnancy or breastfeeding, or intention to become pregnant during the study