For Protocol Amendment #4 to: NRG-GY023

NCI Protocol #: NRG-GY023
Local Protocol #: NRG-GY023

NCI Protocol Version Date: May 23, 2024

This amendment is being submitted in response to an RRA received by Dr. Helen Chen (helen.chen@nih.gov) received on May 9, 2024.

Section	Comment
Footer	NCI Version date is now May 23, 2024
ICD-Drug Risk Section	• Added New Risk: • Rare: Pain and swelling of thyroid

Research Study Informed Consent Document

Study Title for Participants: Comparing Standard of Care Treatment to Three Different Combinations of Drugs

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: (NRG-GY023: A Randomized Phase II Trial of Triplet Therapy (a PD-L1 Inhibitor Durvalumab (MEDI4736) in Combination with Olaparib and Cediranib) Compared to Olaparib and Cediranib or Durvalumab (MEDI4736) and Cediranib or Standard of Care Chemotherapy in Women with Platinum-Resistant Recurrent Epithelial Ovarian Cancer, Primary Peritoneal or Fallopian Cancer Who Have Received Prior Bevacizumab (NCT# 04739800)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer that is resistant to platinum-based chemotherapy and have had prior therapy with bevacizumab.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Do the combinations of durvalumab (MEDI4736) plus olaparib and cediranib, durvalumab (MEDI4736) and cediranib, or olaparib and cediranib keep patients disease free longer than the usual approach?

We are doing this study because we want to find out if these drug combinations are better or worse than the usual approach for your recurrent, platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer. The usual approach is defined as care most people get for your cancer.

What is the usual approach to my ovarian, peritoneal, or fallopian cancer?

The usual approach for patients who are not in a study is treatment with FDA approved drugs.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get usual care non-platinum chemotherapy or one of the three experimental drug treatment combinations with (1) durvalumab (MEDI4736) plus olaparib and cediranib; (2) durvalumab (MEDI4736) and cediranib; or (3) olaparib and cediranib until evidence of disease progression or requirement to stop study participation.

After you finish your treatment, your doctor and study team will watch you for side effects. They will check you every 3 months for 2 years after treatment. After that, they will check you every 6 months for 3 years. This means you will keep seeing your doctor for 5 years after treatment.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study treatment groups may not be as good as the usual approach at treating your cancer.

There is also a risk that you could have side effects from the study drugs used on this study. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Allergic reaction
- Diarrhea
- High blood pressure

- Vomiting, Nausea
- Fatigue

There may be some risks that the study doctors do not yet know about.

Benefits
There is evidence that the combinations of durvalumab (MEDI4736) plus olaparib and cediranib, durvalumab (MEDI4736) and cediranib, or olaparib and cediranib may be effective in stabilizing your type of cancer. It is not possible to know now if the study drugs will extend your time without disease compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?
Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

There are two options of stopping treatment:

1. The first option is that you stop treatment on the study but continue follow up visits (no treatment) to see how you are doing. If you agree to let your study doctor continue to follow you, you will continue to be part of the study so that we can follow you to see how you are doing. We would continue to collect information about how you and your cancer are doing and to see how the treatment affected you and your cancer. This means you would go "off treatment," but not "off study" and you would not withdraw consent to be in this study.

2. The second option is to stop treatment and not allow your study doctor to collect any information on how you and your cancer are doing and how the treatment affected you and your cancer. This is considered "withdrawal of consent" and you would go "off treatment" and "off study".

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?
Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- You become pregnant while on the study.

- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the usual treatment alone to using combinations of durvalumab (MEDI4736), olaparib, and cediranib to increase the duration of time that your cancer does not progress. But it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if any of the 3 different approaches is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the study drugs increase the length of time patients remain progression free compared to the usual approach.

What are the study groups?

This study has 4 groups (Study Groups).

- **Group 1**
  If you are in this group, you will get one of the usual drugs (standard of care) used to treat your type of cancer. The drug will be chosen by you and your physician. It will be one you have not already received. These drugs include one of the following: paclitaxel, Topotecan, or pegylated liposomal doxorubicin. You will receive one of these drugs through a vein in the arm (IV) on a predefined schedule. Each cycle lasts 21 or 28 days depending on the drug chosen. The number of cycles of therapy will be administered as clinically appropriate.

  Combination therapy or addition of a targeted agent are not options on the standard of care arm. There will be about 23 people in this group.

- **Group 2**
  If you are in this group, you will receive durvalumab (MEDI4736) plus olaparib and cediranib to treat your cancer. You will get the durvalumab (MEDI4736) through a vein in the arm, and the olaparib and cediranib in pill form you take by mouth. Each cycle lasts 28 days.

  Durvalumab (MEDI4736), olaparib and cediranib together are not FDA approved for treatment of your disease. There will be about 47 people in this group.

- **Group 3**
  If you are in this group, you will receive durvalumab (MEDI4736) plus cediranib to treat your cancer. You will get the durvalumab (MEDI4736) through a vein in the arm, and the cediranib in a pill form you take by mouth. Each cycle lasts 28 days.

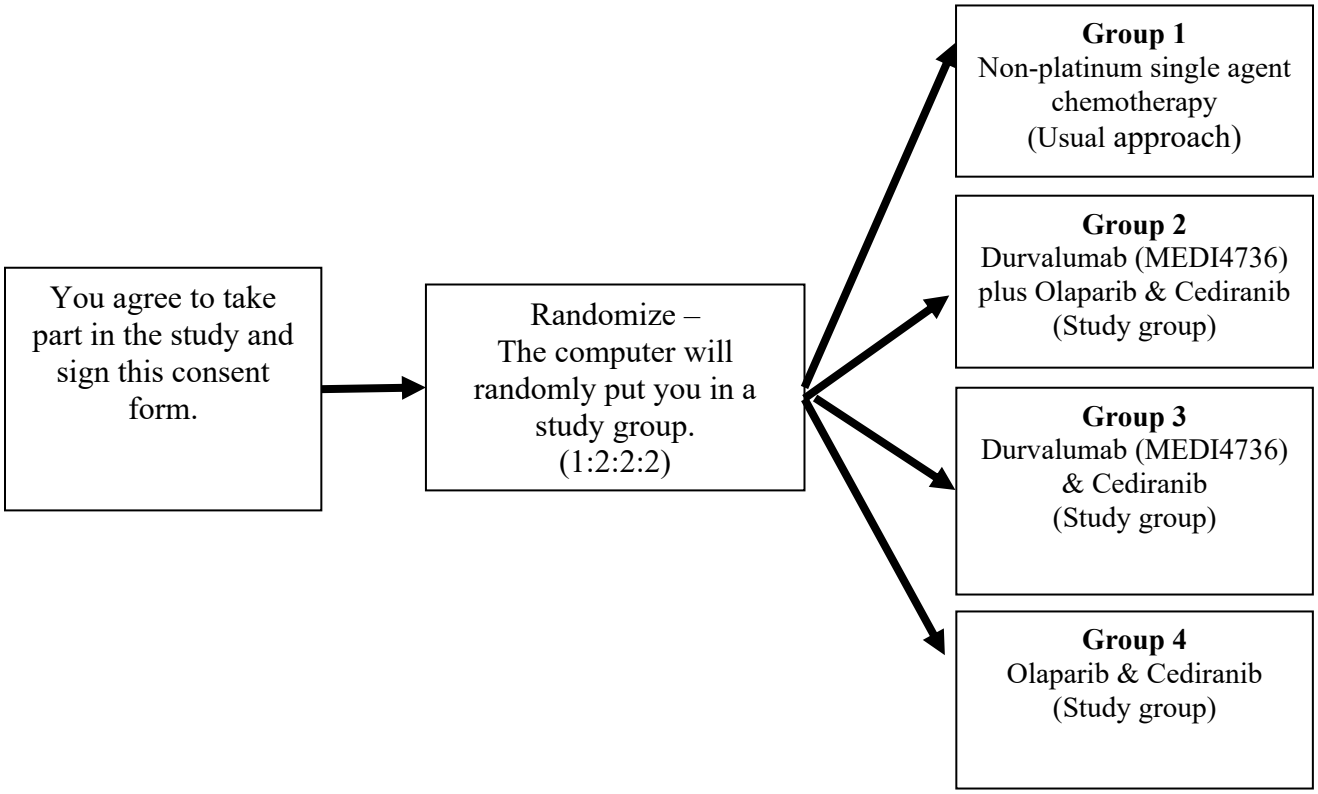
  Durvalumab (MEDI4736) and cediranib are not FDA approved for treatment of your disease. There will be about 47 people in this group.

- **Group 4**
  If you are in this group, you will receive olaparib and cediranib to treat your cancer. You will get both the olaparib and cediranib in a pill form you take by mouth. Each cycle lasts 28 days.

  Olaparib and Cediranib together are not approved by the FDA for treatment of your disease. There will be about 47 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose, and you cannot choose which study group you are in. You will be put into a group by chance. You will be twice as likely to be in Groups 2, 3, and 4 as Group 1.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right. following the lines and arrows.



What exams, tests, and procedures are involved in this study? (27-AUG-2021)

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Additionally, patients receiving cediranib, blood pressure measurements will be required twice daily for 8 weeks after starting the drug. If there are no issues with the blood pressure, the measurements can be reduced to once daily. If high blood pressure medication is required or cediranib is discontinued, continuing twice daily measurements may be required. Blood pressure cuffs and instructions will be provided by your study team for you to be able to measure blood pressure at home.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Your study doctor will need to use some of the tissue left over from a prior biopsy or surgery when you were diagnosed with cancer. You will also a have a tube of blood drawn, for research only, prior to starting study treatment. The blood sample is a required part of the study. Researchers will look for abnormalities (mutations) in your cancer genes. These results might affect your clinical care. You may elect to receive, or to not receive this information. If you choose to receive this information, further testing may be required.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 4 months after your last dose of study drug.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Side Effect Risks
The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.
Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at combination study drugs used to treat this type of cancer. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks
The tables below show the most common and most serious side effects doctors know about for each of the drugs in this study. Your will only be taking the drug(s) used for your group. The drugs are listed alphabetically.

Risk Profile for Cediranib (AZD2171) (Table Version Date: November 7, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving cediranib (AZD2171), more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness • Loss of appetite • Changes in voice • High blood pressure which may cause headaches, dizziness, blurred vision
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving cediranib (AZD2171), from 4 to 20 may have:

• Pain • Constipation, vomiting • Dry mouth • Difficulty swallowing • Sores in the mouth • Infection • Bruising, bleeding • Weight loss • Dehydration • Muscle weakness • Dizziness, headache • Cough, shortness of breath, sore throat • Redness, pain or peeling of palms and soles • Blood clot which may cause swelling, pain, shortness of breath, confusion, or paralysis
RARE, AND SERIOUS In 100 people receiving cediranib (AZD2171), 3 or fewer may have:
• Anemia, kidney problems which may cause tiredness, bruising, swelling, or may require dialysis • Heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or hole in internal organs that may require surgery • Liver damage which may cause yellowing of eyes and skin, swelling • Non-healing surgical site • Damage to the brain which may cause changes in thinking • Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Kidney damage which may require dialysis • Blood clot in artery which may cause swelling, pain, shortness of breath or change of color in extremity

Risk Profile for Durvalumab (MEDI4736) (CAEPR Version 2.5, February 29, 2024)**(23-MAY-2024)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving durvalumab (MEDI4736), more than 20 and up to 100 may have:
• Cough
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving durvalumab (MEDI4736), from 4 to 20 may have:
• Anemia which may require blood transfusion • Pain in the muscles, joints • Diarrhea, nausea, vomiting • Swelling of the body • Tiredness, fever • Infections. Infections can be severe and involve jaws and fatty tissues • Loss of appetite • Painful urination

- Shortness of breath
- Changes in voice
- Increased sweating

Durvalumab (MEDI4736) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Hormone gland problems (especially the thyroid, pituitary and adrenal glands and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Lung problems (pneumonitis and pleural effusion), symptoms may include: new or worsening cough, chest pain, shortness of breath
- Skin: itching; rash; patches of light skin color

RARE, AND SERIOUS

In 100 people receiving durvalumab (MEDI4736), 3 or fewer may have:

- Pain and swelling of thyroid
- Reaction during or after infusion which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Durvalumab (MEDI4736) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Damage to blood cells that may cause bruises and bleeding
- Blood clots in small blood vessels, which may cause kidney failure, fever, and confusion
- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: shortness of breath, swelling of the ankle and body or abnormal heartbeat
- A condition with high blood sugar (diabetes) which leads to tiredness, frequent urination or excessive thirst which may require treatment with insulin
- Swelling and redness of the eye
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Damage to the pancreas which may cause belly pain and hospitalization
- Problem of the muscle (myositis), which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Swelling of the brain, which may cause headache, blurred vision, stiff neck, and/or confusion
- Problem of the nervous system that can cause weakness and paralysis, which may include: numbness, tingling of hands and feet, and may also cause problems with breathing
- Kidney problems, including kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Severe skin reactions with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Liposomal Doxorubicin (Table Version Date: October 17, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Liposomal Doxorubicin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require blood transfusions • Vomiting, nausea, constipation or diarrhea • Sores in mouth which may cause difficulty swallowing • Fever • Weakness, tiredness • Rash • Redness, pain or peeling of palms and soles
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Liposomal Doxorubicin, from 4 to 20 may have:
• Heart attack or failure which may cause chest pain, shortness of breath, swelling of ankles, cough • Blockage of the bowels • Loss of appetite • Reaction during or following infusion of the drug • Headache • Dry eye • Hair loss • Swelling and redness at the site of the medication injection
RARE, AND SERIOUS In 100 people receiving Liposomal Doxorubicin, 3 or fewer may have:
• Severe blood infection • Hepatitis which may cause yellow eyes and skin • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Cancer of bone marrow caused by chemotherapy

Risk Profile for Olaparib (AZD2281) (CAEPR Version 2.6, June 5, 2023) **(27-AUG-2021)(25-JUL-2023)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), more than 20 and up to 100 may have:

• Anemia which may require blood transfusion • Pain • Diarrhea, nausea, vomiting • Tiredness • Loss of appetite
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), from 4 to 20 may have:
• Bloating, constipation, heartburn • Sores in the mouth which may cause difficulty swallowing • Swelling of arms, legs • Cold symptoms such as stuffy nose, sneezing, sore throat • Infection which may cause painful and frequent urination • Infection, especially when white blood cell count is low • Dizziness, headache • Changes in taste • Cough, shortness of breath • Rash
RARE, AND SERIOUS In 100 people receiving olaparib (AZD2281), 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Bruising, bleeding • Cancer of bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Damage to the lungs which may cause shortness of breath • Blood clot

Possible Side Effects of Paclitaxel (Table Version Date: October 14, 2020) **(27-AUG-2021)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Pain • Muscle weakness • Numbness, tingling or pain of the arms and legs • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath
RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Topotecan (Table Version Date: October 17, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Topotecan, more than 20 and up to 100 may have:
• Shortness of breath • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Constipation, diarrhea, nausea, vomiting • Fever • Pain • Tiredness • Hair loss
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Topotecan, from 4 to 20 may have:
• Cough • Blockage of the bowels • Sores in mouth which may cause difficulty swallowing • Headache • Rash

RARE, AND SERIOUS In 100 people receiving Topotecan, 3 or fewer may have:
• Scarring of the lungs • Swelling of the bowels which may require surgery • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Additional Drug Risks
The study drug could interact with other drugs. Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

You should not take herbal-based therapies and multivitamins, medical marijuana, or probiotics oral supplements while on the study treatment and consult the study doctor for guidance.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?
If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

Do not get pregnant or breastfeed while taking part in this study. Tell your study doctor right away if you think that you have become pregnant during the study or within four months after your last dose of study drug.

What are the costs of taking part in this study? (27-AUG-2021)
You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and prevent and treat side effects.
- the cost of the paclitaxel, topotecan, or pegylated liposomal doxorubicin if you are randomized to Group 1.
- the costs of getting the paclitaxel, topotecan, pegylated liposomal doxorubicin, durvalumab (MEDI4736), olaparib, and/or cediranib ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

If you are randomized to Groups 2, 3, or 4, you or your insurance provider will not have to pay for the durvalumab (MEDI4736), olaparib, and/or cediranib while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor, NCI-CTEP, and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research, including NRG Oncology.
- The NRG Oncology Biospecimen Bank-Columbus (Biobank) and laboratories designated by NRG Oncology to perform testing as part of the study.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading this optional study hope the results will help other people in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in this optional study is your choice. You can still take part in the main study even if you say NO to this study. There is no penalty for saying NO. You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Circle your choice of YES or NO for the following study.

Optional storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, any samples remaining after the completion of the study research will be stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG Oncology and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your tumor tissue and blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional storage for possible future studies?
If you agree to take part, here is what will happen next:

1. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
2. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
3. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional storage for possible future studies?
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?
Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?
You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?
There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?
If you decide you no longer want your samples to be used, you can call the study doctor, *(*insert name of study doctor for main trial*)*, at *(*insert telephone number of study doctor for main trial*)*, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?
If you have questions about the use of your samples for research, contact the study doctor, *(*insert name of study doctor for main trial*)*, at *(*insert telephone number of study doctor for main trial*)*.

Please circle your answer below to show if you would or would not like to take part in each optional study.

Samples for unknown future studies
I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

_____

Participant's signature

_____

Date of signature

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature