SUMMARY OF CHANGES

For Protocol Amendment #3 to: NRG-GY021
NCI Protocol #: NRG-GY021
Local Protocol #: NRG-GY021
NCI Version Date: 07/27/2023

Comments Requiring a Response– Administrative & Editorial Issues:

#	Section	Comments
1.	ICD phase II, page 8	Please add back the RARE, AND SERIOUS list for olaparib and include the new risk, "blood clot." **PI Response: Apologies, the list was accidentally cut off when copy/pasting. This is has now been resolved.**

This amendment for NRG-GY021 is being submitted in response to an RRA from Dr. Percy Ivy (ivyp@ctep.nci.nih.gov).

Section	Comments
Footer	NCI Version Date is now July 27, 2023.
What possible risks can I expect from taking part in this study?	Insertion of new Olaparib Risk List: (CAEPR Version 2.6, June 5, 2023) • Added New Risk: • Rare: Blood clot

Study Title for Participants: Testing the addition of an immunotherapy drug, tremelimumab, to the PARP inhibition drug, olaparib, for recurrent ovarian, fallopian tube or peritoneal cancer—Phase II Study

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NRG-GY021, "A Phase II Randomized Trial of Olaparib versus Olaparib plus Tremelimumab in Platinum-Sensitive Recurrent Ovarian Cancer"—Phase II Study (NCT # 04034927)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. 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 platinum-sensitive ovarian, fallopian tube or peritoneal cancer, defined as cancer that has not returned within six months of platinum-containing chemotherapy. You have also had or have agreed to have screening for BRCA mutation status.

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:

Can we lower the chance of your ovarian, fallopian tube or peritoneal cancer growing or spreading by adding an immune therapy drug (tremelimumab) to a PARP inhibitor drug (olaparib)?

We are doing this study because we want to find out if combined therapy with tremelimumab and olaparib is better or worse than treatment with olaparib alone for your recurrent ovarian, fallopian tube or peritoneal cancer.

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

The usual approach for patients with recurrent ovarian, fallopian tube or peritoneal cancer who are not in a study is treatment with more chemotherapy. Chemotherapy drugs that are used for recurrent cancer include carboplatin, paclitaxel, pegylated doxorubicin, and gemcitabine.

Choices about which drugs to use depend on how well prior chemotherapy treatment worked for a particular person. Women who had a remission for at least 6 months after treatment with a type of chemotherapy called a platinum drug (cisplatin, carboplatin or oxaliplatin) are considered to have "platinum-sensitive" disease. For women with platinum-sensitive disease, the usual approach is to administer a platinum drug again in combination with a second chemotherapy drug.

Sometimes, other cancer-directed treatments called targeted drugs may be used to treat recurrent cancer. Targeted drugs selectively kill tumor cells while sparing nearby healthy cells. PARP inhibitors are a type of targeted drug that have been approved by the Food and Drug Administration to treat ovarian cancer. PARP inhibitors are pills that are taken daily. These treatments can reduce symptoms and may stop the tumor from growing for months or longer.

There is not yet evidence that treatment with a PARP inhibitor such as olaparib or the combination of olaparib with tremelimumab being studied in this trial, can offer a similar treatment benefit as standard platinum chemotherapy. However recent studies demonstrate that treatment with olaparib does not lessen the benefit of subsequent platinum chemotherapy.

Your doctor can explain which treatment may be best for you.

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 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 the study drugs olaparib and tremelimumab or you will get olaparib alone. Treatment with the PARP inhibitor, olaparib, will continue for up to two years unless there is evidence that your cancer has grown or you have unacceptable side effects. Treatment with the immune therapy, tremelimumab, will continue for up to two years unless there is evidence that your cancer has grown or you have unacceptable side effects.

After you finish treatment on the study, your doctor will continue to follow your condition and watch you for side effects. They will evaluate your health at clinic visits every 3 months for 2 years after you finish treatment. After that, they will continue to check you with clinic visits

every 6 months for 3 years. This means you will keep seeing your doctor for 5 years after treatment, or until the study ends, depending on which one comes first.

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 combination of olaparib and tremelimumab or olaparib alone may not be as good as the usual approach at shrinking or stabilizing your cancer.

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

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

- Anemia, which may require a blood transfusion
- Diarrhea, nausea, vomiting
- Fatigue
- Loss of appetite
- Rash, itching
- Fever

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

Benefits

There is evidence that the combination of olaparib and tremelimumab is effective in shrinking your type of cancer. It is not possible to know now if the combination of olaparib and tremelimumab will extend your time without disease progression 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.

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 (the National Cancer Institute). 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 treatment with olaparib alone with combined treatment using tremelimumab plus olaparib. The addition of tremelimumab to olaparib could shrink your tumor or prevent it from growing. 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 the combination of olaparib and tremelimumab is better than olaparib alone. To decide if it is better, the study doctors will be looking to see if the combination of olaparib and tremelimumab increases the time without disease progression by 4 months or more compared to treatment with olaparib alone.

This chemotherapy drug, olaparib, is already approved by the FDA for use in ovarian cancer. The immune therapy drug, tremelimumab, has received Orphan Drug Designation, but not Orphan Drug Approval, by the Food and Drug Administration for use in mesothelioma, a rare type of peritoneal or lung cancer. Orphan Drug Designation means it is a drug developed to treat rare conditions.

There will be about 80 people taking part in this study.

What are the study groups?

This study has 2 study groups. You will be told which group you are in.

Group 1
If you are in this group, you will get the usual drug used to treat this type of cancer, olaparib.

Olaparib is a pill. You will take two pills by mouth, twice daily every day until your cancer worsens or you have unacceptable side effects.

There will be about 40 people in this group.

Group 2
If you are in this group, you will get the usual drug used to treat this type of cancer, olaparib, plus a study drug called tremelimumab.

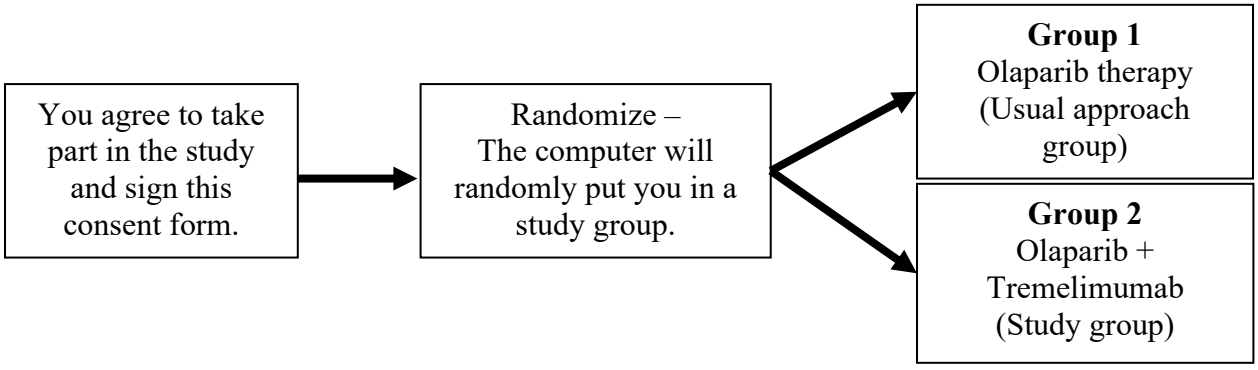
Olaparib is a pill. You will take two pills by mouth, twice daily every day until your cancer worsens or you have unacceptable side effects.

Tremelimumab is given as an infusion through a vein in your arm or an IV port every four weeks. This infusion is administered over 60 minutes. You will get a tremelimumab infusion once every four weeks for four doses, and then once every 12 weeks for up to two years. You will not be able to get additional doses of this drug. This drug is not approved by the FDA for treatment of your disease.

There will be about 40 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 have an equal chance of being in Group 1 or Group 2.

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? (24-APR-2020)

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. This includes CT scans which will be done at 12 weeks after you begin treatment and then every 8 weeks to evaluate the effects of study treatment.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood tests to evaluate thyroid function every 4 weeks if you are in Group 2.

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 your biopsy or surgery when you were diagnosed with cancer and will draw some of your blood at three times during the study. These samples are a required part of the study. These samples will be used to examine how your immune system may respond to your tumor. You and your study doctor will not get the results of this testing.

What risks can I expect from taking part in this study? (27-AUG-2021)

General Risks

If you choose to take part in this study, there is a risk that the combination of olaparib and tremelimumab or olaparib alone may not be as good as other chemotherapy combinations for 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 most common risks related to drawing blood from your arm are brief pain and maybe a bruise.

The olaparib and tremelimumab 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 6 months after you have completed the study.

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.

Genetic Testing Risks

The genetic test used in this study will test your tumor and blood for genetic changes. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. The genetic test used in this study is being done for research purposes only. The results will not be added to your medical records and you or your study doctor will not know the results.

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 a combination of one of the usual drugs used to treat this type of cancer plus a study drug. 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. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects for Olaparib (AZD2281) Group 1 and Group 2 (CAEPR Version 2.6, June 5, 2023) (27-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 lungs which may cause shortness of breath • Blood clot

Myelodysplasia (the occurrence of irreversible abnormal blood counts and bone marrow damage, which may lead to leukemia) has been reported in a small number of patients who have received olaparib. Your study doctor will monitor your blood counts closely while you are on study treatment and may ask you to undergo additional tests if they are concerned you are at risk for developing myelodysplasia.

No studies to establish the effects of Olaparib on the ability to drive and use machinery have been conducted. However, during treatment with Olaparib, weakness, lack of energy, fatigue, and dizziness have been reported and if you experience these symptoms, you should use caution when driving or using machines.

Possible Side Effects of Tremelimumab- Group 2

COMMON, SOME MAY BE SERIOUS In 100 people receiving tremelimumab (CP-675, 206), more than 20 and up to 100 may have:
• Diarrhea Tremelimumab (CP-675, 206) 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: • Skin: itching; dry; rash (may be raised); skin change; hives

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving tremelimumab (CP-675, 206), from 4 to 20 may have:
• Swelling and redness of the eye • Belly pain • Nausea, vomiting • Swelling of arms, legs • Tiredness, fever • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Bruising, bleeding • Infection, especially when white blood cell count is low • Loss of appetite, dehydration • Cough, shortness of breath Tremelimumab (CP-675, 206) 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: • Anemia which may require blood transfusion • 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. • Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine and may require surgery. 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 • Pain or swelling of joints

- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
- Lung problems (pneumonitis). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Kidney damage which may cause swelling, may require dialysis

RARE, AND SERIOUS

In 100 people receiving tremelimumab (CP-675, 206), 3 or fewer may have:

- Damage to the heart
- A condition with high blood sugar which leads to tiredness, frequent urination or excessive thirst
- Dry mouth and dry eyes which may become permanent
- Damage to the skin which may cause tightening and abnormal movement of arms and legs

Tremelimumab (CP-675, 206) 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:

- Swelling of the bowels
- Damage to the pancreas which may cause belly pain and hospitalization
- 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
- Swelling of the brain (encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck
- Swelling of the blood vessels of the scalp which may become severe and may be life-threatening

Because Tremelimumab is administered in the clinic, you will be monitored closely for these symptoms during infusion. ***If you feel any symptoms listed above during or immediately following your infusion, you should alert a nurse or clinician immediately.***
Side effects from tremelimumab may also be delayed. Patients may experience new side effects after the second, third, or fourth treatment with tremelimumab. The most common side effect experienced by patients receiving olaparib and tremelimumab is diarrhea, which is sometimes associated with abdominal pain or cramping. ***If you develop diarrhea, have more frequent bowel movements, or experience other side effects listed above, it is important to notify a nurse or clinician immediately.*** They can advise you about how to manage these symptoms.

Additional Drug Risks

The study drug could interact with other drugs or vaccines.

- Other medications:

- It is important that you tell the medical staff about any other medication you are taking, or thinking of taking, before and during the study, including vitamins, nutritional supplements, herbal or other remedies.
- It is possible that your study medication could affect your other medication and there are certain medications that you will **not** be allowed to take with the study medication during the study including other anti-cancer therapies and certain vaccines.
- There are other medications that should also be avoided if possible, including ketoconazole, itraconazole (used to treat fungal infections), telithromycin, clarithromycin (used to treat bacterial infection), ritonavir, nelfinavir, indinavir, saquinavir, nevirapine (used to treat viral infections, primarily HIV), rifampicin, rifapentine, rifabutin (used to treat bacterial infections, primarily tuberculosis), phenytoin, carbamazepine, phenobarbital (used to treat seizures and epilepsy), modafinil (used to treat a sleep disorder called narcolepsy), St. John's Wort (a herbal remedy used mainly for depression), natural/herbal products and other traditional remedies.

- Vaccines: you must not receive live virus and/or bacterial vaccines (e.g., measles, mumps, rubella vaccine, chickenpox vaccine) while on study treatment and for 30 days after completion of treatment.
- You must not donate blood at any time during the study treatment period and for 3 months afterwards

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.

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

Imaging Risks
The CT scans that you get in this study will expose you to low amounts of radiation. These scans will be done in keeping with standard of care practice, so participation in the study is not expected to increase your exposure to radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

As part of the CT that you get in this study, iodine will be injected into your vein. Some people are allergic to iodine. Let your study doctor know if you have an allergy to iodine or seafood or if you have kidney problems. If you have an allergy to iodine, it will not be used as part of the CT scan.

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 6 months after your last dose of study drug.

What are the costs of taking part in this study?

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 costs of getting the tremelimumab 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, nurse, or other staff for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- Submission of tumor tissue from your previous surgery or biopsy
- The collection of extra blood at three times during the study

You or your insurance provider will not have to pay for the olaparib or tremelimumab while you take part in this study.
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 or any drug 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.

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 these optional studies hope the results will help other people with cancer 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 these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no". You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies:

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 blood and/or tissue remaining after the study testing is completed will be stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG 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 blood and/or tissue 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.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample storage?

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 sample storage?

- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- 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[s]*) at (*insert telephone number, and email address if appropriate*), 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[s]*) at (*insert telephone number, and email address if appropriate*).

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 Printed Name _____

Participant's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion

Printed Name _____

Signature**:** _____

Date of signature _____