NRG ONCOLOGY

NRG-LU006

(ClinicalTrials.gov NCT #04158141)

PHASE III RANDOMIZED TRIAL OF PLEURECTOMY/DECORTICATION PLUS SYSTEMIC THERAPY WITH OR WITHOUT ADJUVANT HEMITHORACIC INTENSITY-MODULATED PLEURAL RADIATION THERAPY (IMPRINT) FOR MALIGNANT PLEURAL MESOTHELIOMA (MPM)

Amendment 2: April 13, 2022

Research Study Informed Consent Document

(15-MAR-2022)
Study Title for Participants: Testing the addition of targeted radiation therapy to surgery and the usual systemic therapy treatment for malignant pleural mesothelioma (MPM)

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NRG-LU006, "Phase III Randomized Trial of Pleurectomy/Decortication Plus Systemic Therapy With or Without Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy for Malignant Pleural Mesothelioma (MPM)," (NCT #04158141)

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 malignant pleural mesothelioma (MPM), cancer in the lining of the lungs, and you are a candidate for a type of surgery called pleurectomy/ decortication that involves removing the affected lung lining and all visible masses, but not the affected lung itself.

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? (15-MAR-2022)
This study is being done to answer the following question: Can we extend your life by adding a type of radiation therapy that targets the lining of the lung to the usual treatment of surgery and chemotherapy? This type of radiation avoids the healthy lung tissue as much as possible and could extend your life.

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your cancer. The usual approach is defined as care most people get for MPM.

What is the usual approach to my malignant pleural mesothelioma? (15-MAR-2022)

The usual approach for patients who are not in a study is treatment with surgery and chemotherapy. Recently, the Food and Drug Administration (FDA) approved immune therapy treatment in MPM. The chemotherapy drugs used in this study are approved by the FDA and commonly used with lung surgery. For patients who get the usual approach for this cancer, about 60 patients out of 100 live longer than one year.

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? (15-MAR-2022)

If you received chemotherapy and/or immune therapy before entering the study:
If you decide to take part in this study, you will have surgery.

If you have not received any treatment before entering the study:
If you decide to take part in this study, you will have surgery followed by 12 weeks of chemotherapy.

All Participants:
After you finish your study treatment, your doctor will reevaluate you to see if you can still take part in this study. If you no longer meet the study criteria after surgery and chemotherapy, your participation in the study will end. If you meet study criteria you will get placed in one of the two study groups. One group will receive radiation therapy and one group will not.

For all participants, your doctor will continue to follow your condition for about 5 years and watch you for side effects. They will see you in the clinic every 3 months for 2 years, then every 6 months for 3 more years.

What are the risks and benefits of taking part in this study? (15-MAR-2022)

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 usual approach plus radiation therapy may not be as good as the usual approach alone for helping you live longer.

There is also a risk that you could have side effects from the radiation treatment. These side effects are in addition to and different from those you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:
- Tiredness
- Peeling of skin
- Sores in esophagus (swallowing tube) which may cause temporary difficulty swallowing
- Cough
- Shortness of breath
- Infection
- Nausea, vomiting
- Loss of appetite or weight loss
- Anemia

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

Benefits
There is evidence that adding radiation therapy to surgery and drug therapy may be effective in stabilizing your type of cancer. It is not possible to know now if the addition of radiation will extend your life 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. This may mean slowly stopping the chemotherapy and the radiation therapy so that there is not a sudden unsafe change, risk to your health, etc. 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.
- For women: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NRG Oncology). 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? (15-MAR-2022)

The purpose of this study is to compare the usual treatment alone to having radiation that targets the diseased area of the lung lining and avoids the healthy lung tissue as much as possible plus the usual treatment. The addition of this radiation therapy to the usual treatment could help you live longer. 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 this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the study approach increases the life of patients by 6 months or more compared to the usual approach.

What are the study groups? (15-MAR-2022)

This study has two study groups.

All study participants will have surgery.

- Participants who received chemotherapy and/or immune therapy before enrolling in the study will have surgery 4-8 weeks after the last drug therapy.

- Participants who did not receive chemotherapy and/or immune therapy before enrolling in the study will get the usual chemotherapy drugs used to treat this type of cancer 4-8 weeks after surgery. You will get these drugs through a vein in the arm every 3 weeks for up to 4 cycles. Each cycle lasts 21 days.

It does not matter what order you have these treatments (surgery followed by chemotherapy or chemotherapy and/or immunotherapy before study enrollment then surgery once you enroll), but you must have both types of treatment.

Four to eight weeks after you complete surgery and chemotherapy you will be assigned to one of the study groups.

- **Group 1**
  If you are in this group, your treatment will be complete and you will be carefully monitored by the doctor and regularly assessed.

  There will be up to 70 people in this group.

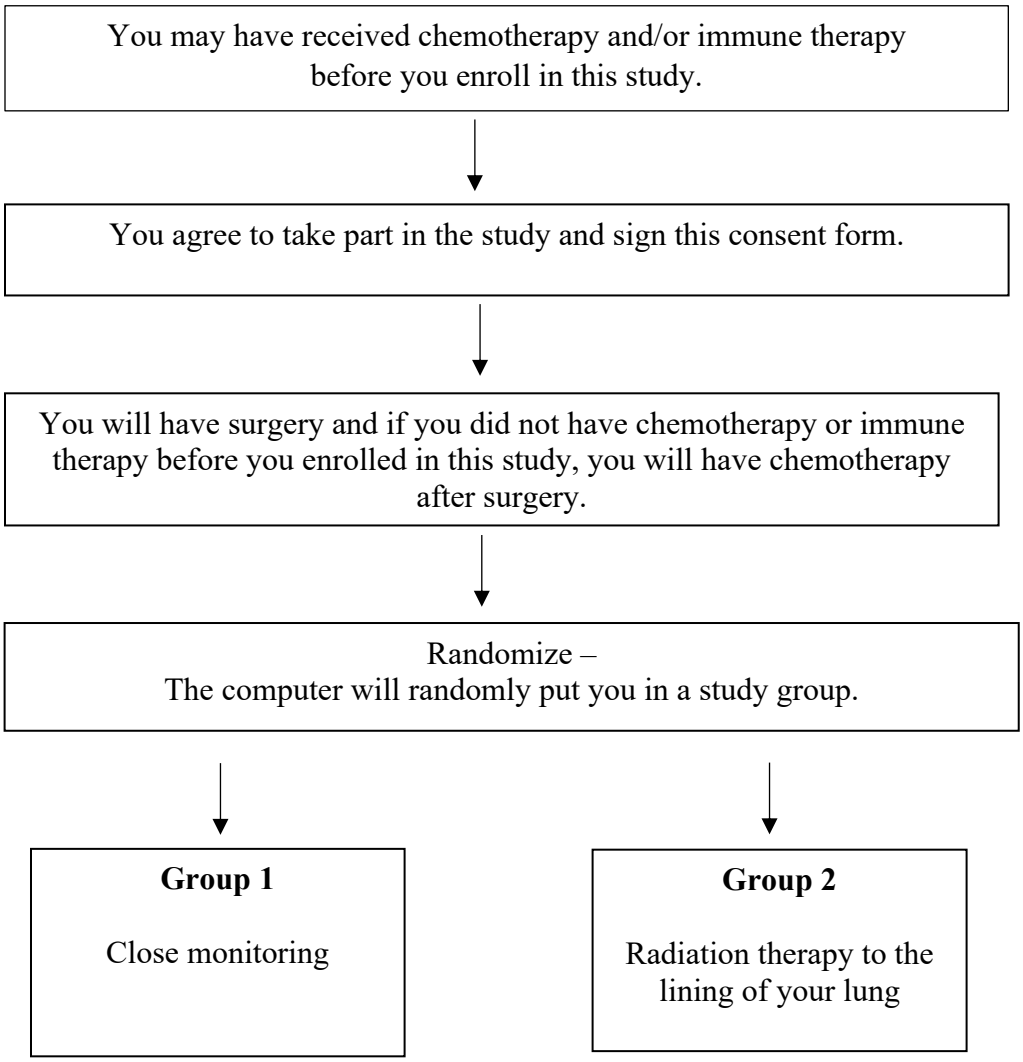
- **Group 2**
  If you are in this group, you will receive radiation to the lining of your lung 5 days/week for about 6 weeks. You will be carefully monitored by the doctor and regularly assessed.

  You will not get additional doses of drugs during this time, or radiation after the 6 weeks.

There will be up to 70 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 top and read to the bottom, following the lines and arrows.



What exams, tests, and procedures are involved in this study? (15-MAR-2022)

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.

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.

Quality of Life Study
If you speak and understand English, Spanish or French, you will be asked to fill out 2 forms with questions about your physical and emotional well-being. Researchers will use this information to better understand how patients feel during treatments and what effects the treatments are having.

Since these forms are being used for research, the responses you provide will not be shared with your study doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

If you received drug therapy before starting the study, you will be asked to fill out these forms 6 times as follows:

- Before surgery
- After surgery
- At 3, 9, 15 and 21 months after randomization

If you did not receive drug therapy before starting the study, you will be asked to fill out these forms at 7 times as follows:

- Before surgery
- After surgery before drug therapy
- After surgery and drug therapy
- At 3, 9, 15 and 21 months after randomization

Each form will take about 5 minutes to complete for a total of 10 minutes to complete the forms each time. The forms will ask about your overall health, your ability to do activities, and things like tiredness and shortness of breath. You don't have to answer any question that makes you feel uncomfortable.

What risks can I expect from taking part in this study? (15-MAR-2022)

General Risks
If you choose to take part in this study, there is a risk that the usual treatment plus radiation therapy may not be as good as the usual approach for your cancer 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.

The chemotherapy and radiation therapy 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 1 month after you have completed the study. You

must let your study doctor know about any pregnancy that occurs at any time during the study and within 6 months after you have completed the study.

Side Effect Risks
The drugs and radiation therapy 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 surgery.

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.

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.

Study Group 1 and Group 2 – Possible side effects of pemetrexed, cisplatin and carboplatin are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Possible Side Effects of Pemetrexed (Table Version Date: June 3, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Pemetrexed, more than 20 and up to 100 may have:
• Nausea, loss of appetite, weight loss • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Pemetrexed, from 4 to 20 may have:
• Damage to the lungs which may cause shortness of breath • Scarring of the lungs • Swelling of the body • Infection, possibly in the blood, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Kidney damage which may cause swelling, may require dialysis • Sores in mouth which may cause difficulty swallowing • Constipation, vomiting, diarrhea, belly pain • Radiation Recall Syndrome which may cause swelling and redness of the area of radiation • Numbness and tingling of the arms and legs • Fever • Rash, itching, blisters, peeling of skin • Hair loss

RARE, AND SERIOUS In 100 people receiving Pemetrexed, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Blockage of the bowels • Stevens-Johnson syndrome which may cause severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Cisplatin (Table Version Date: August 6, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Kidney damage which may cause swelling, may require dialysis • Hearing loss including ringing in the ears • Nausea, vomiting • Confusion • Numbness, pain and tingling of the fingers, toes, arms and/or legs, loss of balance

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, from 4 to 20 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Diarrhea • Change in taste • Hair loss

RARE, AND SERIOUS In 100 people receiving Cisplatin, 3 or fewer may have:
• Brain damage, Posterior Reversible Encephalopathy syndrome, which may cause headache, seizure, blindness • Seizure • A new cancer, including leukemia, resulting from treatment of a prior cancer

Possible Side Effects of Carboplatin (Table Version Date: October 18, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Vomiting, nausea • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, constipation, belly pain • Changes in taste • Numbness and tingling in fingers and toes • Weakness • Swelling, redness, and pain at the site of the medication injection

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Visual loss • Difficulty hearing

Study Group 1 and Group 2 – Possible side effects of surgery are listed in the table below. This surgery is part of the usual approach for treating this type of cancer:

SURGERY:
Common side effects of surgery include (but are not limited to) pain, bleeding, infection, wound healing difficulties, and injury to surrounding areas. The table below lists some of the common side effects of surgery depending on the type and location of your surgery. Prior to your surgery, you will need to sign a surgical consent form provided by your doctor, which is separate from this trial and specific to the type of surgery you will undergo. The surgical consent will include risks specific to the type and location of your surgery. When you sign the surgical consent and during discussions with your surgeon, you should ask your surgeon about those risks.

COMMON, SOME MAY BE SERIOUS In 100 people undergoing surgery, more than 20 and up to 100 may have:
• Nausea, anorexia (loss of appetite) • Pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people undergoing surgery, from 4 to 20 may have:
• Damage to the liver may result in liver damage that can causes yellowing of the skin and eyes, bleeding/bruising, fluid in the abdominal, tiredness, confusion, and itching • Bleeding • Infection • Lung collapse • Fluid around the lungs • Wound healing difficulties • Swelling of the body • Injury to the nerves causing numbness

RARE, AND SERIOUS In 100 people undergoing surgery, 3 or fewer may have:
• Prolonged need to be on a breathing machine with a breathing tube in place, and/or prolonged need to have a tube in the chest because of damage to the lung • Injury to the areas near the site of surgery including: ▪ Injury to the bowels resulting in the need for a "bag" so that the bowels drain outside of the body ▪ Kidney damage ▪ Pancreas injury

Study Group 2 - In addition to side effects listed above, people who are in Group 2 may also have some side effects from the radiation therapy. These side effects are listed below.

Possible Side Effects of Lung Radiation

COMMON, SOME MAY BE SERIOUS In 100 people receiving lung radiation, more than 20 and up to 100 may have:
• Swelling and redness, tanning, thickening, numbness, or peeling of the skin in the area of radiation • Difficulty and/or pain with swallowing • Hair loss in the treatment area, may be permanent • Shortness of breath • Cough with or without increased phlegm production • Tiredness • Diarrhea, nausea • Anemia, which may require blood transfusion • Infection, especially when white blood cell count is low • Bleeding, bruising • Rib pain, increased risk of rib fracture

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving lung radiation, from 4 to 20 may have:
• Inflammation of the lung that may cause difficulty breathing and can be life-threatening • Narrowing of the throat which may cause vomiting, difficulty swallowing • Scarring in the lung • Lung collapse • Fluid around lungs • Bleeding from the lungs which may cause coughing up blood • Fever • Narrowing of the esophagus • Pain in chest wall

RARE, AND SERIOUS In 100 people receiving lung radiation, 3 or fewer may have:
• Abnormal opening in internal organs which may cause pain and bleeding • Irritation of the heart causing heart failure, heart attack, chest pain, abnormal heartbeat, shortness of breath, swelling of ankles, cough or tiredness • Transverse myelitis – irritation of the spinal cord causing weakness, tingling or numbness of the lower body and legs, or paralysis of the lower half of the body • Brachial plexopathy – irritation of the nerves controlling the arm, causing weakness or paralysis • Bleeding from the airway (windpipe) • Narrowing of the airway causing shortness of breath • Death • Lung damage, may be life threatening • Damage to the large blood vessels surrounding the heart, which could cause coughing up of blood and possibly death • Sores and skin damage causing bleeding and severe pain and may lead to an open wound

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.

For women: Do not get pregnant or breastfeed while taking part in this study and for one month after end of treatment. **For men:** Do not father a baby while taking part in this study and for 1 month after end of treatment. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 months after completing the study.

What are the costs of taking part in this study? (15-MAR-2022)

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 surgery, the chemotherapy drugs (if you are receiving chemotherapy after surgery), and if you are in Group 2, the radiation therapy.
- 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 research coordinator 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:

- Quality of life assessments.

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:

- NRG Oncology and any company supporting the study now or in the future.
- 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 Food and Drug Administration and the groups it works with to review research.
- The NCI and the groups it works with to review research, including the Cancer Trials Support Unit (CTSU).
- The NCI's National Clinical Trials Network and the groups it works with to conduct research.

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.

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 your type of 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 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 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 sample collections for known laboratory studies and/or storage for possible future studies (15-MAR-2022)

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, blood will be collected from a vein in your arm and stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG Oncology and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. 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. 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 collection?
If you agree to take part, here is what will happen next:

1. After you enroll in this study, about 4 tablespoons of blood will be collected from a vein in your arm before treatment prior to surgery, after randomization (before radiation for participants in Group 2), and at your 3 month follow up visit. A sample from the tissue that was collected at the time of your surgery will be sent to the biobank.

2. 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.
3. 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.
4. 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 collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- 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 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 _____