Research Study Informed Consent Document

Study Title for Participants: Testing the addition of the immunotherapy drug, pembrolizumab, to the usual radiation treatment for newly diagnosed early stage high intermediate risk endometrial cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol NRG-GY020, "A Phase III Randomized Trial of Radiation +/- Pembrolizumab (MK-3475) for Newly Diagnosed Early Stage High Intermediate Risk Mismatch Repair Deficient (dMMR) Endometrioid Endometrial Cancer (NCT # 04214067)"

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 endometrial cancer which has been determined to have certain risk factors. Your tumor has been tested, and is mismatch repair deficient (dMMR). DNA mismatch repair (MMR) is a system for recognizing and repairing DNA errors and damage. You may have acquired this over the course of your life, but in 2-3% of endometrial cancers this may be due to a hereditary disease called Lynch Syndrome (previously called hereditary nonpolyposis colorectal cancer or HNPCC). Tumors that have evidence of mismatch repair deficiency tend to be more sensitive to immunotherapy. However, immunotherapy is currently only approved for endometrial cancer if the cancer has come back after receiving chemotherapy.

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 endometrial cancer coming back by adding an immunotherapy drug to the usual treatment with radiation?

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

What is the usual approach to my endometrial cancer?

The usual approach for patients who are not in a study is treatment with surgery, followed by vaginal radiation called vaginal brachytherapy. Sometimes pelvic radiation (external beam radiation) is used and sometimes chemotherapy is used. If you and your doctor plan on using chemotherapy, you are not eligible for this study. For patients who get the usual approach for this cancer with similar features to yours, about 80 out of 100 are free of cancer after 3 years. There is no FDA approved treatment for early stage high intermediate risk endometrial cancer.

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 get either radiation for 2-6 weeks or you will get radiation for 2-6 weeks and immunotherapy through a vein in your arm every 6 weeks for up to one year, unless your cancer returns sooner or the side effects become too severe. The type of radiation you receive, vaginal brachytherapy in which a cylinder placed inside your vagina will deliver the radiation, or pelvic external beam radiation, will be decided by you and your doctor before you begin the study. The decision about which type of radiation treatment to use is not part of this study; your radiation oncologist and gynecologic oncologist will decide this together with you.

After you finish your 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.

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 addition of pembrolizumab may not be as good as radiation alone at preventing your cancer from coming back.

There is also a risk that you could have side effects from the addition of pembrolizumab. 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:

- Skin problems
- Fatigue
- Diarrhea
- Autoimmune reactions (abnormalities in liver, pancreas, kidney and lung function)
- Rash
- Thyroid dysfunction
- Shortness of breath
- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise

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

Benefits

There is evidence that immunotherapy is effective in shrinking or stabilizing endometrial cancer after it has come back. We do not know at this time if the immunotherapy (pembrolizumab) will reduce the risk of your cancer coming back compared to the usual approach (radiation only). 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 with immunotherapy or radiation, but you would 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 and if your cancer comes back. 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 is considered that you go "off treatment" but not "off study" and you would not withdraw consent.

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.
- 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 (radiation) to using the usual treatment plus pembrolizumab (immunotherapy). The addition of pembrolizumab to the usual treatment could reduce the risk of your cancer coming back. 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, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if the addition of pembrolizumab to radiation treatment reduces the risk of your cancer coming back from approximately 20% to approximately 5% at 3 years.

This immunotherapy drug, pembrolizumab (Keytruda®), is already approved by the FDA for use in several other types of cancer (e.g. melanoma, lung cancer, kidney cancer, bladder cancer, head and neck cancers, and also in cervical cancer and endometrial cancer that has come back after treatment with chemotherapy).

There will be about 168 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 radiation therapy with vaginal brachytherapy. If you have Stage IB grade 3 or Stage II endometrial cancer, your doctor may recommend pelvic external beam radiation.

  Vaginal brachytherapy consists of 3-6 outpatient treatments over the course of approximately 2-3 weeks. The treatment is delivered by placing a cylinder inside the vagina through which radiation can be delivered. The treatment itself lasts just a few minutes, but your radiation doctor will also require additional time to take extra imaging to make sure the radiation is delivered properly to the right area.

  If your doctor recommends pelvic radiation, you will get daily (outpatient) external beam radiation (Monday to Friday) for five to six weeks.

  If you join this study, and are in Group 1 you will not be able to receive a live, attenuated vaccine (a weakened form of a live virus) for 4 weeks leading up to treatment, and for the first 3 months after beginning the study. Examples include vaccines for measles, mumps and rubella (MMR), chickenpox (varicella), and intranasal influenza (e.g., Flu-Mist®).

  There will be about 56 people in this group.

- **Group 2**

  If you are in this group, you will get radiation therapy with vaginal brachytherapy. If you have Stage IB grade 3 or Stage II endometrial cancer, your doctor may recommend pelvic external beam radiation.

  Vaginal brachytherapy consists of 3-6 outpatient treatments over the course of approximately 2-3 weeks. The treatment is delivered by placing a cylinder inside the vagina through which radiation can be delivered. The treatment itself lasts just a few minutes, but your radiation doctor will also require additional time to take extra imaging to make sure the radiation is delivered properly to the right area.

  If your doctor recommends pelvic radiation, you will get daily (outpatient) external beam radiation (Monday to Friday) for five to six weeks.

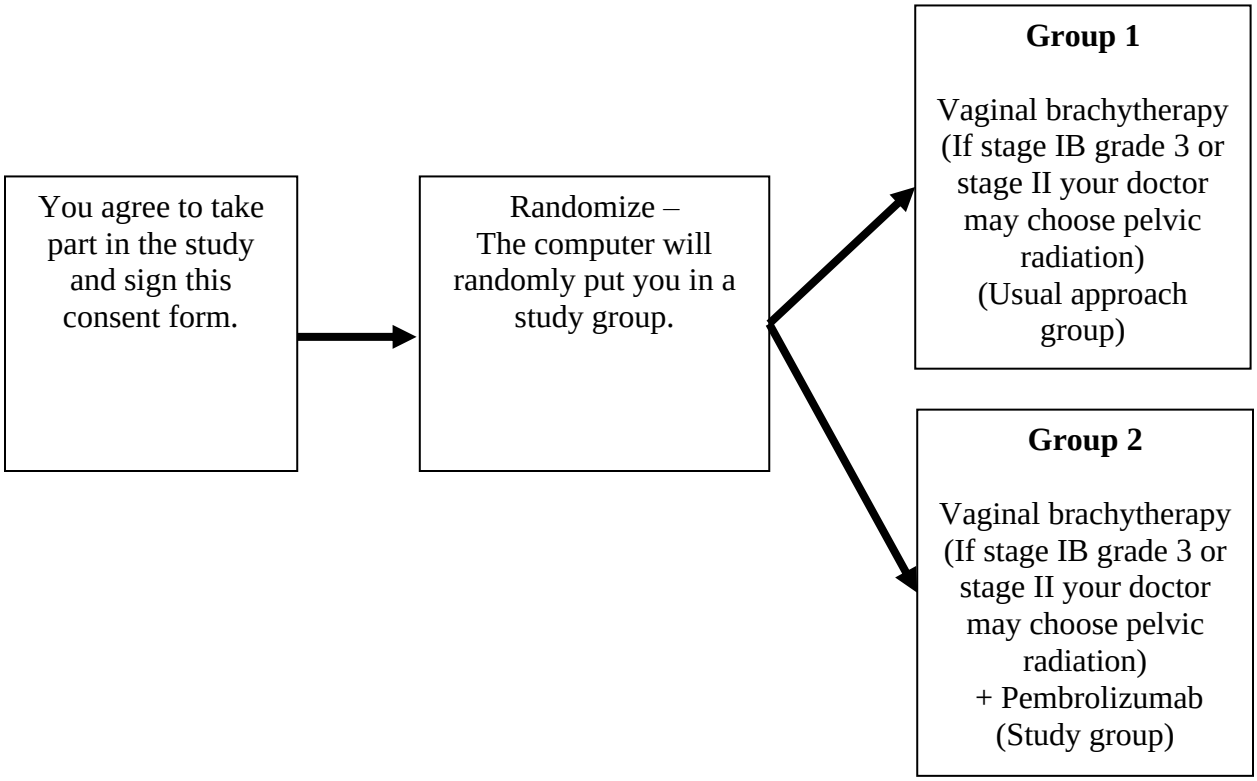
  You will also receive a study drug called pembrolizumab. You will get pembrolizumab through a vein in the arm over approximately 30 minutes starting the week before you begin radiation and then on the first day of each cycle. Each cycle lasts 6 weeks. You will continue to receive pembrolizumab once every 6 weeks for up to 1 year (9 cycles). If you began treatment on this study when the pembrolizumab was given every 3 weeks, you will switch to an every 6-week schedule after your next scheduled 3-week treatment.

If you join this study and are in Group 2, you will not be able to receive a live, attenuated vaccine (a weakened from of a live virus) for 4 weeks leading up to treatment, and for the year you will be getting pembrolizumab. Examples include vaccines for measles, mumps and rubella (MMR), chickenpox (varicella), and intranasal influenza (e.g., Flu-Mist®). Certain shingles vaccines are allowed (not live-attenuated) and you should confirm with your doctor before getting this. You will not be allowed to take steroids (while on pembrolizumab) without talking to your study doctor.

There will be about 112 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 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?

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 every six months for the first three years and then every twelve months for the next three years to evaluate the effects of study treatment.

This study will use genetic tests that may identify changes in the genes in your DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. The researchers are looking at these changes for research purposes only. You and your doctor will not be notified of the results.

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.
- Your study doctor will also collect about 2 tablespoons of your blood at two times during the study. These samples are a required part of the study and will be used to examine the diversity of your immune cells. You and your study doctor will not get the results of this testing.

If you speak and understand English, Spanish or French and choose to take part in this study, you will be asked to complete a survey with questions about your well-being, how you are feeling and symptoms you may be having. These questions are called “quality of life” or “patient-reported outcomes” (PRO) questions. Researchers will use this information to learn more about how cancer and cancer treatment affects people. The surveys are a mandatory part of the study, but you don’t have to answer any question that makes you feel uncomfortable.

Your personal smart phone or tablet, or if available a tablet provided at your health care clinic, will be used to enter your answers to the survey questions. The use of your own electronic device on a cellular network may result in a nominal cost to your data plan. Regardless of the device you use, your answers and personal information will not be stored on the device. Your survey answers will be sent to the research database and will be kept private in the same way listed in the section about who will see your medical information. Your e-mail address will only be used for this survey study and will not be used for mail or marketing purposes.

You will be asked to fill out this survey at 5 different times and each time it will take about 10 minutes to complete:

- Before you begin treatment
- At approximately 6 weeks after starting treatment
- At approximately 24 weeks after starting treatment
- At approximately 1 year after starting treatment
- At approximately 2 years after starting treatment

If you need help using the survey application on your phone or tablet, ask for help at your treatment site. You don't have to answer any question that makes you feel uncomfortable. You may have an alternate person complete the survey on your behalf if needed, and you will need to provide that information on the survey.

Since this is a research survey, the responses you provide will not be shared with your doctor. If you are having any severe symptoms, health issues or other concerns, please be sure to discuss these with your doctor or nurse right away.

If using your phone or a tablet is not possible, a paper survey will be provided.

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 addition of pembrolizumab to radiation may not be better than radiation alone at preventing your cancer from coming back.

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.

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 to examine the diversity of your immune cells. 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.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the test results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Side Effect Risks

The radiation and drug 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 radiation and drug.

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 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 / Radiation 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 Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, 20 to 100 may have:
• Mild pain • Tiredness • Diarrhea • Nausea

- Anemia which may require blood transfusion
- Narrowing and/or shortening of the vagina
- Vaginal dryness

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving radiation therapy, 4 to 20 may have:

- Sores or ulcers in the vagina or on the skin
- Discomfort when you urinate
- Discomfort in the vagina
- Discomfort in the rectum and/or with bowel movements
- Rectal bleeding

RARE, AND SERIOUS
In 100 people receiving radiation therapy, 3 or fewer may have:

- Damage to internal organs (bowels, bladder, rectum)
- Abnormal opening in internal organs which may cause pain and bleeding
- Abnormal opening between organs (vagina, bladder, rectum, bowel) called fistula

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

Possible Side Effects of MK-3475 (Pembrolizumab) (25-FEB-2020)

COMMON, SOME MAY BE SERIOUS
In 100 people receiving MK-3475 (pembrolizumab), more than 20 and up to 100 may have:

- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving MK-3475 (pembrolizumab), from 4 to 20 may have:

- Nausea
- Infection
- Loss of appetite
- Pain in back
- Joint stiffness
- Cough
- Swelling and redness of the skin

MK-3475 (pembrolizumab) 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
- Pain in lymph nodes
- Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness

- 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. 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
- Diarrhea
- Sores in the mouth which may cause difficulty swallowing
- Pain in belly
- Sores in the bowels
- Chills, fever
- 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
- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Fluid in the joints
- Pain in chest
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives

RARE, AND SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), 3 or fewer may have:

- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

MK-3475 (pembrolizumab) 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:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body
- Swelling and redness of the eye
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin

- Damage to organs in the body when the body produces too many white cells
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in a coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures, and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Swelling or tenderness of blood vessels

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Additional Drug Risks

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 to monitor if your cancer has come back will expose you to low amounts of 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 scans that you get in this study, you will get oral contrast to drink and 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.

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.

Do not breastfeed while taking part in this study.

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 endometrial 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 pembrolizumab ready and giving it to you (if you are in Group 2).
- 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 study 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:

- The submission of tissue and blood samples for research.

If you are in Group 2, you or your insurance provider will not have to pay for the pembrolizumab 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. Contact information for your study doctor is listed on the consent cover page. 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.

No funds have been set aside to compensate you in the event of injury.

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:

- Montana Cancer Consortium
- 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, including the Cancer Trials Support Unit (CTSU).
- The NCI's National Clinical Trials Network and the groups it works with to conduct research, including NRG Oncology and the Imaging and Radiation Oncology Core (IROC).
- 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 information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

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 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 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.

Known future studies

If you choose to take part in this optional study, any tissue and blood samples remaining after completion of the main study research will be stored. These samples will be used for research to understand how your immune system responds to your tumor.

Unknown future studies

If you choose to take part in this optional study, any tissue and blood samples remaining after completion of the main study research and the known research described above 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. 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 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.
- 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 storage?

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 storage?

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 storage ?

If you decide you no longer want your samples to be used, you can call the study doctor who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. 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 storage ?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

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

Samples for known future studies:

I understand and agree that my samples and related health information may be used for the laboratory study described above.

YES NO

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 Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)

(Required for initial consent only)