Research Study Informed Consent Document

Study Title for Participants: Testing the addition of the immunotherapy drug pembrolizumab to the usual chemotherapy treatment (paclitaxel and carboplatin) in endometrial cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NRG-GY018, A Phase III Randomized, Placebo-Controlled Study of Pembrolizumab (MK-3475) in addition to Paclitaxel and Carboplatin for Measurable Stage III or IVA, Stage IVB or Recurrent Endometrial Cancer (NCT # 03914612) (09/24/2019)

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 and your tumor has been tested for mismatch repair (MMR) deficiency.

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 growing or spreading by adding a new immunotherapy drug to the usual combination of chemotherapy drugs?

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, radiation, or drugs including: carboplatin, paclitaxel, gemcitabine, pegylated liposomal doxorubicin, and topotecan (all U.S. Food and Drug Administration [FDA] approved agents;). Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer. The usual approach is proven to help patients with your health condition live longer.

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

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

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

If you decide to take part in this study, you will first have a sample of your tumor that was removed during a previous surgery or biopsy sent to NeoGenomics to see if your cancer tissue has mismatch repair (MMR) deficiency. Although you have already had such a test done, all patients on this study will have the same test done at NeoGenomics. This will make sure that the testing is done in the same way for everyone. This test is done to determine whether your tumor is pMMR (MMR proficient) or dMMR (MMR deficient). This information will NOT impact the treatment you receive; this information will be used to make sure there are a certain number of patients with pMMR and dMMR assigned to each treatment group. NeoGenomics will also test your tumor for expression of programmed-death ligand 1 (PD-L1). This is a marker that is expressed on the surface of some cancer cells, and its expression may help predict response to immunotherapy drugs. This testing will not impact the treatment you receive or your ability to enroll on this trial.

Everyone in the study will get either paclitaxel and carboplatin with pembrolizumab or paclitaxel and carboplatin with a placebo for four and a half months, followed by only pembrolizumab or only a placebo for up to two years. Placebo looks like the study drug but contains no medication. Neither you nor your doctor(s) will know which treatment you are receiving--this is called a blinded study. The study is blinded to prevent bias when the outcomes of the different treatments

are measured. The placebo group provides an important baseline with which to compare the treatment group, and helps increase confidence in interpretation of the results of the clinical trial.

You will be able to find out whether you received pembrolizumab or placebo, a process called unblinding, in the following circumstances:

1. If you experience a serious medical problem and the researchers determine that the information is needed to treat your problem.
2. You or your physician feel that your safety may be affected by COVID-19 in your local/home area, areas of travel, or your doctor's office and/or treatment center. You can request, after discussion with your physician, to find out if you are on pembrolizumab or placebo. If you were receiving pembrolizumab, you can continue your pembrolizumab maintenance. If you are uncomfortable continuing pembrolizumab maintenance, you may elect to withdraw consent for treatment. If you do that, you would be encouraged to remain on the study for continued follow-up. If you were receiving placebo, you would be encouraged to remain on the study for continued follow-up. This follow-up is every 6 weeks for in-person visits with your physician, and every 12 weeks for reassessment imaging. We understand that this can be a difficult decision and will respect the decision you make.
3. If your tumor is found to grow/progress on therapy you may request unblinding. Pembrolizumab alone (if you have mismatch repair deficient disease) or pembrolizumab with lenvatinib (if your disease is mismatch repair intact) would be an approved treatment if you have not already received pembrolizumab in this study.

If you meet one of the above criteria, your doctor will use the group's standard unblinding process to find out what your blinded treatment assignment is. You can ask your doctor at any time to explain this process to you. If your treatment is unblinded for any of the reasons as listed, you will still participate in the study follow up as described below.

After you finish your study treatment, your doctor and study team will continue to follow your condition and watch you for side effects during clinic visits or by phone if you are unable to visit the clinic. They will check you every 3 months for 2 years after treatment. After that, they will check you every 6 months for 3 years. This means you will keep seeing your doctor for up to 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 better than the usual approach at shrinking or stabilizing your cancer.

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

Some of the most common side effects that the study doctors know about, observed with the standard chemotherapy, and the study drug are:

- Allergic reaction
- Infection
- Hair loss
- Vomiting, Nausea
- Fatigue
- Autoimmune reactions (i.e. abnormalities in liver, pancreas, kidney and lung function)
- Rash
- Thyroid dysfunction
- Inflammation of the colon with diarrhea
- Dyspnea
- Constipation

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

There also may be risks associated with coming in for medical evaluations followed by either pembrolizumab or placebo, due to the COVID-19 pandemic. Some evidence suggests that individuals with cancer may be at increased risk of becoming seriously ill if they get infected by SARS-CoV-2, the virus that causes the pandemic disease known as COVID-19.

Benefits

There is evidence that adding pembrolizumab to standard chemotherapy is effective in shrinking or stabilizing certain cancers. It is not possible to know now if the pembrolizumab will extend your time without disease compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

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

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

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

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

What is the purpose of this study?

The purpose of this study is to compare the usual treatment of paclitaxel and carboplatin to the combination of paclitaxel, carboplatin and pembrolizumab. Because the study includes a placebo, patients will be randomly assigned to receive paclitaxel plus carboplatin plus pembrolizumab or paclitaxel plus carboplatin plus placebo. The addition of pembrolizumab to the usual treatment could shrink or stabilize your cancer. 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 usual treatment prolongs the time your cancer is in remission, or the duration of time you are alive after treatment when compared to the usual approach.

This immunotherapy drug, pembrolizumab, 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 other cancers). In previous clinical trials, the addition of pembrolizumab to chemotherapy has significantly prolonged the interval of time that patients live without their cancer growing back, and the amount of time they are alive after treatment.

There will be about 810 people taking part in this study.

What are the study groups?

This study has 2 study groups. You will not be told which group you are in.

- **Group 1**

  If you are in this group, you will get a placebo plus the usual drugs used to treat this type of cancer (paclitaxel and carboplatin). The placebo solution looks like the study drug, but contains no medication. You will get these drugs through a vein in the arm or via a port

every 3 weeks for 6 cycles (combination phase of the trial). You will continue to receive this treatment through a vein in the arm or via a port on the first day of each cycle. Each cycle lasts 3 weeks. After the combination portion of the study, you will enter the maintenance phase. In the maintenance phase, you will undergo medical evaluation followed by placebo alone through a vein in the arm or via a port on the first day of each 6-week cycle for up to 14 more cycles (a total of 2 years).

There will be about 405 people in this group.

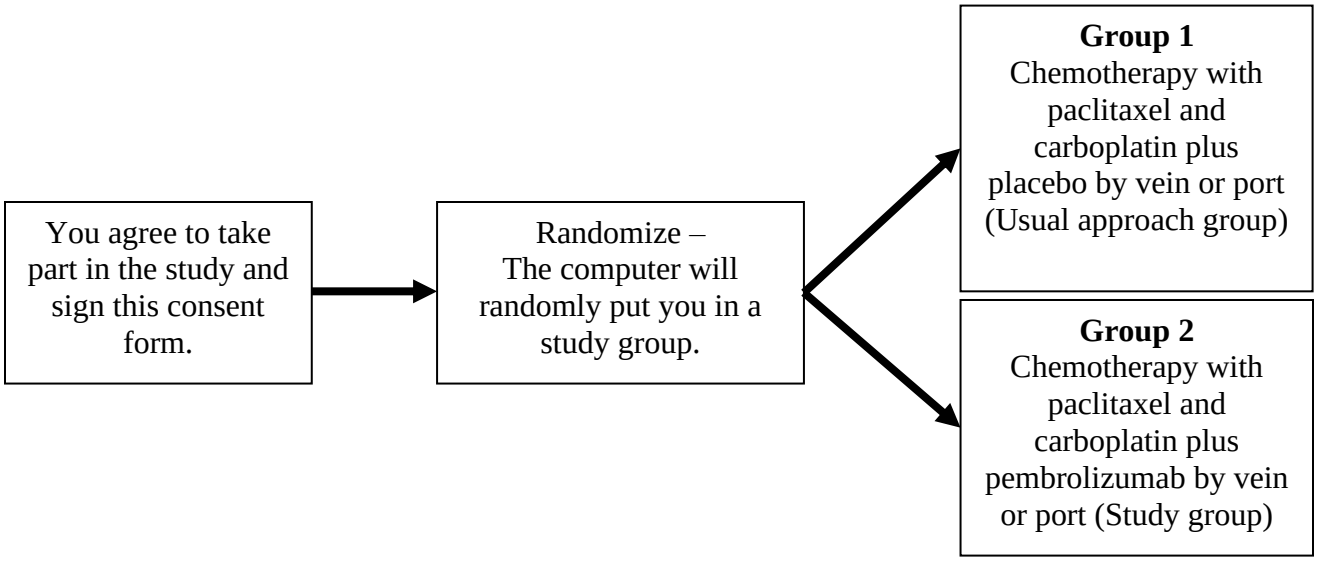
- **Group 2**

  If you are in this group, you will get a study drug called pembrolizumab plus the usual drugs used to treat this type of cancer (paclitaxel and carboplatin), through a vein in the arm or via a port every 3 weeks for 6 cycles (combination phase of the trial). You will continue to receive this treatment through a vein in the arm or via a port on the first day of each cycle. Each cycle lasts 3 weeks. After the combination portion of the study, you will enter the maintenance phase. In the maintenance phase, you will undergo medical evaluation followed by pembrolizumab alone through a vein in the arm or via a port on the first day of each 6-week cycle for up to14 more cycles (a total of 2 years).

  There will be about 405 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?

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.

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:

- Thyroid testing done before treatment and then every other cycle.

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. This sample is a required part of the study. This sample will be used to confirm whether the tumor tissue has proteins related to a type of abnormality in how your tumor and cells repair damage in your genes. You and your study doctor will get the results of this testing. If the results of this testing suggest a possible abnormality in these genes, your study doctor may recommend that you undergo germline testing to exclude an inherited genetic predisposition to cancer called Lynch Syndrome. Your study doctor may also refer you to a genetic counselor for discussion and to complete genetic testing. It is important to know that identifying the abnormality in the tumor tissue is not the same as having an inherited genetic predisposition to cancer, and alone is not informative about future cancer risk for the patient or family. Your study doctor will refer you for genetic counseling and testing if deemed clinically appropriate.

If you choose to take part in this study, you speak and understand English, Spanish or French, and your tumor is pMMR (MMR proficient) 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.

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 up to 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 18 weeks after starting treatment
- At approximately 30 weeks after starting treatment
  At approximately 54 weeks 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 may not be better than the usual approach at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.
- Potential increased risk of exposure to COVID-19. During the maintenance phase, you will undergo medical evaluation followed by pembrolizumab or placebo every 6 weeks.

The chemotherapy (paclitaxel, carboplatin) and immunotherapy (pembrolizumab) used in this study could be very harmful to an unborn or newborn baby. You should not get pregnant or breastfeed a baby while in this study. 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.

Women of child-bearing potential must agree to use adequate contraception (barrier or hormonal method of birth control; abstinence) prior to study entry and for the duration of study participation through 4 months after receiving the last treatment. If you become pregnant while receiving treatment on this study, you should inform your doctor immediately.

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

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.

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 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 of Paclitaxel

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

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Carboplatin

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

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Bruising, bleeding • Belly pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, Constipation • Numbness and tingling in fingers and toes • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Changes in taste • Changes in vision

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Damage to organs which may cause hearing and balance problems

Possible Side Effects of MK-3475 (Pembrolizumab)

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.

When used in combination (chemotherapy + pembrolizumab), patients may experience any of the above listed side effects. Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

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 4 months after your last study treatment.

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 the paclitaxel and carboplatin.

- The costs of the 14 maintenance infusion visits over the two-year maintenance period, which may be for the study drug or for the placebo.
- the costs of getting the paclitaxel, carboplatin and pembrolizumab or placebo 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.

You or your insurance provider will not have to pay for the pembrolizumab or placebo while you take part in this 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.

Although you or your insurance company will need to pay the cost of the maintenance visits that include the infusions (pembrolizumab or placebo), you and/or your insurance provider will not have to pay for any other exams, tests and procedures done for research purposes only, or that are covered by the study. These include:

- Submission of tumor tissue and blood for research.

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.
- 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 this optional study hope the results will help other people in the

future. The results will not be added to your medical records and you or your study doctor will not know the results.

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

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

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

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

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

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- 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?

- 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. (~For non-US participants, adapt the following two sentences as needed. ~) 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 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)