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RUTGERS
Cancer Institute
of New Jersey
RUTGERS HEALTH

Rutgers, The State University of New Jersey
195 Little Albany Street
New Brunswick, NJ 08903-2681

cinj.org
p. 732-235-2465

CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: A Basket Trial of Pembrolizumab in Patients with Advanced Solid Tumors and Genomic Instability

PRINCIPAL INVESTIGATOR: Eugenia Girda, MD
Rutgers Cancer Institute of New Jersey
195 Little Albany Street
New Brunswick, NJ 08903

STUDY-RELATED PHONE NUMBER(S): 732-235-2465 (24 hours)

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

The study doctor, Eugenia Girda, MD, or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Even after signing this consent form, you may withdraw from the study at any time.

Sponsor of the study

The Rutgers Cancer Institute of New Jersey is the sponsor of this study. Merck & Co., Inc will supply the study drug, Pembrolizumab (MK-3475) and is providing funding support.

Why is this study being done?

This study is being done to test effects of the study drug called pembrolizumab when given to patients with either a POLE and POLD1 mutations or BRCA1/2 mutations (a change in DNA sequence of cells). POLE, POLD1 and BRCA1/2 are genes (pieces of DNA containing information for a specific purpose or job). They are responsible for:

- The POLE and POLD1 genes are involved in the repair and replication of DNA.
- The BRCA1/2 genes are involved in controlling the growth of cells

Pembrolizumab is a PD-1 inhibiting drug and has been approved by the FDA to treat melanoma, lung cancer, and head and neck cancer and certain other cancers. Depending on the type of cancer

you have, pembrolizumab may not have been approved for your cancer and therefore may be experimental. "Experimental" means that the study drug is currently being tested and it is not approved by the U.S. Food and Drug Administration (FDA) for treatment of your condition. Typically, the human body's immune system recognizes abnormal cells in the body and destroys them. Cancer cells frequently create proteins on the cell surface (PD-L1) that act as signals to turn off this part of the immune system. Pembrolizumab is a drug that blocks (inhibits) this signal on the immune system's cells (PD-1) and allows the immune system to recognize these cancer cells as foreign.

Why have you been asked to take part in this study?

You are being asked to take part in this study because you have an advanced cancer with POLE and POLD1 mutations or BRCA1/2 mutations. Advanced cancer means that the cancer is either:

- Metastatic (spread to other parts of the body than where it started)
- Recurrent (was previously treated, but has returned)
- Locally advanced (cannot be removed by surgery)

Who may take part in this study? And who may not?

You may be eligible to take part in this study if you are 18 years of age or greater with an advanced solid tumor. Additionally, you may take part in this study if:

- You have either POLE and POLD1 mutations or BRCA1/2 mutations
- You have tumor available from a previous surgery or biopsy
- You have read and signed this Informed Consent Form

You may not take part in this study if:

- You are unable to keep your doctor's appointments
- You are pregnant or breast feeding

How long will the study take and how many subjects will participate?

You will continue to receive treatment with pembrolizumab for approximately 24 months so long as you are able to tolerate it. After you have stopped receiving treatment on study, we will continue to follow up with you for the rest of your life.

A total of approximately 46 patients will take part in this study nationally.

What will you be asked to do if you take part in this research study?

Before you begin study treatment:

You will have some exams, tests and procedures to find out if you can take part in this study. Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, your doctor will do some extra testing as part of the study. Procedures not part of regular medical care are marked with an asterisk (*). The testing that you will need to have if you take part in this study is discussed below. If some of these have been done recently they may not need to be repeated, this will be up to the study doctor.

- Your age and race/ethnicity will be recorded.
- You will be asked about your medical history and any medications you are currently taking, both prescription and over the counter.

- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- The following blood samples will be collected within 14 days of registration:
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney and liver function tests to ensure that it is safe to administer any of the drugs included in this study
    - Approximately 1 teaspoon (5 mL) for blood clotting tests
    - Approximately 1 teaspoon (5 mL) for thyroid function testing
- If you are a woman who could become pregnant (even if you had a tubal ligation), your doctor will perform a blood or urine pregnancy test. If you are pregnant, you cannot participate in this study.
- Urinalysis which looks at your urine to see if you have a problem with your kidneys or an infection
- Imaging tests typically performed for cancer patients. Scans will include:
    - Computed tomography (CT), a scan that uses x-rays to look at one part of your body. It may be done with or without contrast. Contrast means that dye is injected into your vein to increase the differences between normal and abnormal tissue.
    - Magnetic resonance imaging (MRI), imaging that uses a strong magnetic field to look at one part of your body.
- **Research Collection of Tumor:* You will be asked to provide a sample of your tumor for research from a prior surgery or biopsy. If your tumor specimen is unavailable, you will undergo a biopsy to collect a tumor sample for research.

  Your doctor will send the tumor sample to a central lab for testing of certain proteins and biomarkers (indicators of normal biological or disease processes) to understand the nature of your disease and its response to treatment with pembrolizumab. These laboratory tests are new and under development.

If you do not meet the eligibility requirements, you cannot take part in this study. The study doctor will inform you of other options that are available to you.

STUDY TREATMENT

If the tests, exams, procedures show that you can be in the study, you will be enrolled. All study participants will receive treatment with pembrolizumab.

Pembrolizumab will be given Day 1 of every 3 week cycle. It will be given by IV through a vein over about 30 minutes.

<u>While on study treatment:</u>

During the treatment period, you will need the following examinations, tests, and procedures

described below. Some of these exams, tests, and procedures are part of your regular medical care. Procedures not part of regular medical care are marked with an asterisk (*).

You will have the following on Day 1 of every 21 day cycle while receiving pembrolizumab alone:

- You will be asked to report any symptoms and health problems you have and any new medications you have started.
- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- You will have blood tests:
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney, and liver function tests.
    - Approximately 1 teaspoon (5 ml) for thyroid function tests
- *Tumor Assessments:* You will have a CT or MRI scan every 9 weeks until Cycle 8, then every 12 weeks to evaluate how your cancer is responding to the treatment.
- **Research Labs:* In addition to blood tests required to monitor your health, other blood tests will be done for research. An additional 6 teaspoons (30 mL) will be collected prior to starting treatment, after 4 weeks of treatment, then an additional 4 teaspoons (20 mL) every 6 weeks.

**Research Biopsy:* An optional biopsy will be done after 4 weeks of treatment. The tumor will be sent to a central laboratory for testing and will not be a part of your medical record.

<u>After you have completed study treatment:</u>

Your doctor will stop study treatment if any of the following occur:

- Your tumor grows larger or you develop new tumors (disease progression)
- You develop unacceptable side effects
- You become pregnant or are unwilling to use appropriate birth control techniques
- The study doctor determines that it is not in your best interest to continue the study treatment
- You have completed study treatment as planned and your disease has not worsened
- New information becomes available
- The study is stopped by the Sponsor, Merck & Co., Inc., & the IRB or FDA
- You choose to stop study treatment

<u>Safety Follow-Up</u>

After all study treatment has stopped, your doctor will ask you to return to the clinic for an end of treatment visit. Procedures not part of regular medical care are marked with an asterisk (*).You will return for another clinic visit approximately 30 days after your last dose of study drug. The following assessments will be done at these visits:

- You will be asked to report any symptoms and health problems you have and any new medications you have started.

- You will have a complete physical examination, with your physician or physician's assistant, including measurement of your vital signs (breathing rate, blood pressure, temperature, and heart rate), height, and weight.
- Evaluation of your ability to carry out daily activities.
- You will have blood tests (at the 30 day post-treatment visit):
    - Approximately 2 teaspoons (10 mL) for routine testing, such as, a complete blood count, kidney, and liver function tests.
    - Approximately 1 teaspoon (5 ml) for thyroid function tests
- **Research Labs:* In addition to blood tests required to monitor your health, other blood tests will be done for research. An additional 6 teaspoons (30 mL) will be at the time of progression of disease.
- **Research Biopsy:* A tumor biopsy will be done at the time of progression of disease. The tumor will be sent to a central laboratory for testing and will not be a part of your medical record.
- If you discontinue study treatment for any reason other than progression, you will have imaging tests every 12 weeks; unless you discontinued after Cycle 8 then scans will be done every 16 weeks.

Follow-Up
If you have any ongoing side effect at the time you complete the study or your doctor discontinues you from the study, the study doctor will continue to follow your condition until the side effect resolves or becomes stable.

If you discontinue study treatment for any reason other than progression, you will have imaging tests every 12 weeks; unless you discontinued after Cycle 8 then scans will be done every 16 weeks.

The study staff will contact you approximately every 12 weeks after the safety follow up visit to check on your health status. If they are not able to reach you, they may use a public information source (like county records) to obtain information about your survival status only, which will be reported as part of the data for the study.

<u>Second Course Treatment:</u>

You may be eligible for up to one year of additional pembrolizumab (MK-3475) therapy if the disease progresses after stopping pembrolizumab (MK-3475). Your study doctor will determine if you meet the study criteria to be eligible for the Second Course Treatment. If you are eligible, you will restart treatment at the dose and dose frequency received upon initial treatment with pembrolizumab (MK-3475).

What are the risks and/or discomforts you might experience if you take part in this study?

You may have side effects from the drugs or procedures used in this study, and they will vary from person to person. Study doctors will carefully watch everyone taking part in the study for

any side effects. However, the study doctors and the study funders do not know all the side effects that may happen, and unknown side effects that could occur. The study doctors may give you medicine to help lessen the side effects. In some cases, side effects can be serious, long lasting, and/or may never go away. There also is a rare risk of death. You should talk to your study doctor about any side effects that you have while taking part in the study.

If you experience any severe side effect, you should:

- Seek professional medical help immediately
- Call your study doctor
- If necessary, go to the nearest emergency room

Side Effects of Pembrolizumab

Pembrolizumab which is approved in the *USA and* some other countries is available by prescription to treat several different cancers, but may not be approved to treat your type of cancer.

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 serious (i.e., causing hospitalization or be life-threatening), and 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.

Very Common

Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

Common

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Fever
- Back pain
- Rash
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, or have infrequent or hard stools (hypothyroidism)
- Low level of salt in the blood that may cause you to feel tired, feel confused, have a headache, have muscle cramps and/or feel sick to your stomach (hyponatremia).

Uncommon
Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:
* The term inflammation is used below. "Inflammation" means a localized physical condition in which part of the body becomes reddened, swollen, hot, and often painful.

- Inflammation of the lungs; so you may feel short of breath and cough (pneumonitis).
- Too much thyroid hormone so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism).
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut , which may cause severe pain in your belly with loose or watery stools and black, tarry, sticky stools or stools with blood or mucus (colitis).
- Inflammation of the skin so you may have peeling of the skin, itchiness and/or skin redness. The skin inflammation (i.e. peeling, itching, and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome/or toxic epidermal necrolysis).

Rare
Out of 100 people who receive pembrolizumab, less than 1 person may have the following:
- Inflammation of the nerves that may cause pain, weakness or tingling your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (Guillain-Barre syndrome).
- Inflammation of the muscles so you may feel weak or have pain in your muscles (myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe upper abdominal pain that may move to your back, feel sick to your stomach, and have vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye so you may have eye redness blurred vision, sensitivity to light, have eye pain, see floaters or have headaches (uveitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting (hypophysitis).
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle, and belly aches, nausea, vomiting, diarrhea, fever, salt craving, and sometimes darkening

of the skin like a suntan (adrenal insufficiency).

- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots.
- Inflammation of the kidney, so you may pass less urine or have cloudy or bloody urine, swelling and low back pain (nephritis)
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis).
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis).
- A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing (myasthenic syndrome/myasthenia gravis including exacerbation).
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example; if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue.

Additionally, since pembrolizumab as was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis).
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis).
- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-

Koyanagi-Harada syndrome)

- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GVHD), which may include diarrhea, skin rashes, and liver damage, **after receiving pembrolizumab**. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

Patients treated with pembrolizumab **BEFORE** going on to receive an allogeneic stem cell transplant (a procedure in which a person receive blood –forming stem cells from a donor), should inform their transplant physicians that they have received pembrolizumab in the past.

In patients with any hematologic malignancy (cancer of the blood like Hodgkin lymphoma, multiple myeloma), there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab **BEFORE** an allogeneic stem cell transplant.

Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver, and gastrointestinal symptoms), including death, have been received for patients who received pembrolizumab **BEFORE** an allogeneic stem cell transplant.

Patients with multiple myeloma who were treated with pembrolzumab in combination with either pomalidomide or lenalidomide (drugs related to thalidomide which affect the body's immune system) and dexamethasone (a steroid) had an increased number of side effects and deaths as compared to patients who received only dexamethasone and either pomalidomide or lenalidomide.

<u>Risks Associated with Biopsies</u>

- Pain and discomfort at the biopsy site
- Minor bleeding at the biopsy site
- Tenderness at the biopsy site
- Scarring at the biopsy site
- Rarely, an infection at the biopsy site.

Reproductive risks

You should not become pregnant or father a baby while on this study because the drugs and radiation treatment in this study can affect an unborn baby. Women who are able to have children will have a pregnancy test before beginning treatment. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control for as long as you are receiving treatment on this study and for 120 days after completion of all treatment to prevent pregnancy or fathering a child. Check with your study doctor about what kind of birth control methods to use. Some methods might not be approved for use in this study. The treatment in the study may make you unable to have children in the future. Women of childbearing age can ask their doctor for information about pre-treatment or post-treatment reproductive or fertility options prior to agreeing to participate in the study.

Possible Risks Related to Reproductive health/sexual activity

Researchers have not studied the effect of the study drug, pembrolizumab, on human sperm and eggs. They also do not know the effects on the developing fetus using the study drug during pregnancy and the risk of birth defects from use of pembrolizumab. Therefore, both men and women should not attempt pregnancy and women should not be pregnant or breast-feeding while taking part in this study and for at least 120 days after your last dose of the study drug pembrolizumab.

If sexually active, both men and women should use an effective method of birth control while taking the study drug. Barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUDs), hormonal contraceptives, oral contraceptive pills, surgical sterilization, and complete abstinence are examples of effective methods. Only methods that use condoms provide reasonable/true protection against sexually transmitted diseases. If you or your partner become pregnant while taking the study drug, you must tell your study nurse/doctor immediately. You may have to stop the study drug. Your doctor will discuss other treatment options with you if you stop the study drug.

A woman should not breast-feed a baby while in this study because pembrolizumab may enter the breast milk and possibly harm the child.

If you are a woman capable of bearing children, you will have a pregnancy test before you can participate in this study. If at any time during the study or within 120 days after your last dose of the study drug pembrolizumab you suspect that you have become pregnant, please notify the study doctor immediately.

Male participants should immediately inform the study doctor if your partner becomes pregnant during the study, within 120 days after your last dose of the study drug pembrolizumab.

Are there any benefits for you if you choose to take part in this research study?

Taking part in this study may or may not make improve your health better or allow you to live longer. The information from this study will help doctors learn more about pembrolizumab as a treatment for patients with cancer with POLE and POLD1 or BRCA1/2 mutations. This information could help other people who have a similar medical condition in the future.

What are your alternatives if you don't want to take part in this study?

You do not have to take part in this research study. If you decide not to take part in this study, you have other choices. Instead of being in this study, you can:

- Other chemotherapy treatments
- Take part in another study
- Get comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Standard of care options may include specific chemotherapies or molecularly targeted therapies, the utility of which depend on your tumor's organ of origin and molecular profile. Please consult your physician to understand which, if any, alternatives may exist for the treatment of your cancer.

How will you know if new information is learned that may affect whether you are willing to stay in this research study?

During the 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. When informed of this new information, if you agree to continue in the study, your doctor will ask you to sign an updated Informed Consent Form.

Will there be any cost to you to take part in this study?

You will have tests and procedures that are part of your regular medical care (not part of the research), including the treatment with chemotherapy and radiation therapy. You or your insurance company or third party provider will be responsible for these costs, including co-payments and deductibles. You will not be responsible for the cost of research related assessments (blood collected for research purposes only and biopsies done for research purposes only).

The study will provide the drug pembrolizumab at no charge to you while you take part in this study. The study does not pay for the cost of getting the study drug ready and giving it to you intravenously (in a vein). You or your insurance company will pay for this procedure.

Your doctor and your other health care providers will bill the cost of your regular medical care to you or to your health insurance company in the usual way. However, some health insurance plans will not pay the costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular treatment. If your insurance does not pay, you will be responsible for the charges of your regular medical care. Before you decide to participate in the study, you should check with your health insurance company to find out exactly what it will pay for.

If you have any questions about insurance coverage, including any out of pocket expenses you might incur, or which laboratory or facilities you are allowed to have tests at, a financial counselor will be made available to you upon request.

Will you be paid to take part in this study?

You will not receive any payment for your participation in this study.

How will information about you be kept private or confidential?

All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. Your personal information may be given out if required by law.

Information about your cancer and treatment will be collected from your medical record for the study. The information will be with a study identification number and stored in a secured electronic file. The electronic file is password protected and accessible only to authorized study personnel.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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

What will happen if you are injured during this study?

Subjects in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, which were discussed in the Risk and Discomforts section of this consent form. In addition, it is possible that during the course of this study, new adverse effects of pembrolizumab that result in personal injury may be discovered. The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

You are not giving up any of your legal rights by signing this informed consent form or by taking part in this research study.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

You can decide to stop at any time. If you decide to stop for any reason, you must let the study doctor know as soon as possible so you can stop safely.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

It is important to tell the study doctor if you are thinking about stopping so any risks from the

study can be evaluated by your doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

In addition, the study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to:

Eugenia Girda, MD
Rutgers Cancer Institute of New Jersey
195 Little Albany Street
New Brunswick, NJ 08901
Telephone: (732) 235-2465

At any time, the study doctor can take you out of this study because it would not be in your best interest to stay in it, even if you are willing to stay in the study.

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?

If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:

Eugenia Girda, MD
Rutgers Cancer Institute of New Jersey
195 Little Albany Street
New Brunswick, NJ 08901
Telephone: (732) 235-2465

If you have any questions about your rights as a research subject, you can call:
IRB Director
(732)-235-9806 New Brunswick/Piscataway

What are your rights if you decide to take part in this research study?

You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

Please note: This section of the informed consent form is about additional research that is being

done with people who are taking part in the main study. You may take part in this additional research if you want to. You can still be a part of the main study even if you say 'no' to taking part in this additional research.

OPTIONAL BIOPSY

If you agree a biopsy will be used to determine how the immune system is responding to the treatment. The optional biopsy will be done after 4 weeks of treatment. The tumor will be sent to a central laboratory for testing and will not be a part of your medical record.

Risks Associated with Optional Biopsies

- Pain and discomfort at the biopsy site
- Minor bleeding at the biopsy site
- Tenderness at the biopsy site
- Scarring at the biopsy site
- Rarely, an infection at the biopsy site.

Request to Store Leftover Tissue* Samples for Future Research Use

*We use the term "tissue" to refer to specimens such as blood, urine, existing already taken tumor tissue from a previous surgery before entering this study, or tissue taken from a surgery as part of this research study.

We ask your permission to store left over tissue samples collected from you during a previous surgery and/or during this study for future research. Following are details about our request. Please know that you may still participate in the main study even if you say no to this request to store tissue for future research.

How and where will your leftover tissue be stored and by whom?

Your leftover tissue samples will be stored in the Cancer Institute of New Jersey Biorepository Service (BRS), which is owned and operated by the Rutgers Cancer Institute of New Jersey. The repository is at 195 Little Albany Street, New Brunswick, NJ, 08903.

The purpose of the repository is to store leftover tissue samples to be used for future research to be conducted by the Principal Investigator and the research staff at Cancer Institute of New Jersey. The goal of the research is to better understand and develop better means to prevent, diagnose and treat disease.

All of the subjects in this study will be asked to allow leftover tissue to be stored and used for future use in the repository. The more samples and health information available in storage, the more useful the repository will be for medical research.

How will samples be collected?

Only the leftover tissue that was collected during a previous surgery and/or as a part of this research study for future research would be stored and used for future use.

Psychological or Social Risks Associated with Loss of Privacy:

While the databases developed for this project will be coded to protect your personal information, people may develop ways in the future that would allow someone to link your medical information back to you. It is also possible that there could be violations to the security of the computer systems.

There also may be other privacy risks that we have not foreseen.

What are the benefits of participation?

You will not benefit personally from providing tissue samples for this tissue bank because research usually takes a long time to produce meaningful results. However, your participation may help investigators understand, prevent, or treat the diseases and conditions studied in the future.

How will information about you and your tissue samples be kept private and confidential?

Information obtained from this research with material obtained from your tissue sample(s) will be kept confidential so that neither the investigator nor the Sponsor can link your individual research results with your identity.

Your sample(s), and materials derived from your sample(s), will be given a code number, and only information related to your age, sex, race, health condition and other relevant clinical information collected in the main study will be linked with the sample's code number. Your name, date of birth, address, or other personal identifying information, will not be linked with the sample(s) you give.

Is there other important information to consider?

Yes. There is no cost to you to allow us to store and use your tissue and information for future research. Nor will you be paid to participate in this repository. Should any products or services result from research using your samples and information, there is no plan to share any of the profits with you.

The research we are doing is only a stepping stone in understanding disease. It may take a long time for our research to produce useful health-related information. Therefore, tests done for our research using your samples and information will not be useful in directing your medical care. Information from our research will not be returned to you, your family members, your doctor, or outside parties. It is possible, however, that members of regulatory authorities, such as the U.S. Food and Drug Administration, Rutgers University Institutional Review Board, or other persons required by law may be allowed to look at this information.

What are your rights if you agree to the storage and use of your tissue for future research?

You have the right to ask questions about any part of our storage and future research at any time. You should not sign this form unless you have a chance to ask questions and have been given answers to all of your questions. Your participation in this part of the study is voluntary. You do not have to participate. If you do, you can change your mind at any time.

What are the procedures for withdrawing consent?

If you agree to allow your tissue to be stored for future research at the Rutgers Cancer Institute of New Jersey Biorepository Service, but change your mind later, you can write to your study doctor, Eugenia Girda, MD, Rutgers Cancer Institute of New Jersey, 195 Little Albany Street, New Brunswick, NJ 08903 and tell him to destroy any remaining tissue samples and data that are currently being stored in the repository.

However, please note that it may not be possible to destroy samples, information and data created from your samples that may have already been used in research studies prior to your request. The Rutgers Cancer Institute of New Jersey will keep records linking your identity with the tissue sample(s) indefinitely. Until those records are destroyed, you may ask that your tissue sample(s) and materials obtained from your sample(s) be destroyed.

PLEASE INITIAL ONE OF THE FOLLOWING:

You may choose not to have this procedure if you do not want to. You may still be enrolled in this study if you say no.

_____ I agree to have a biopsy of my tumor after 4 weeks of treatment.

_____ I do not agree to have a biopsy of my tumor.

Permission to Collect Leftover Tissue if you have an optional biopsy:

Please read each sentence below and think about your choice. After reading each sentence, initial next to "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our research review board at 732-235-9806.

No matter what you decide to do, it will not affect your care or your participation in the main study.

Any leftover tissue (from research blood or research biopsies) may be collected and stored for research to learn about, prevent or treat cancer

_____YES _____NO

Permission to Contact You with Additional Requests to Participate in Research

Please tell us if we may contact you in the future to tell you about other ways you may participate in this research or other research we are conducting by initialing next to your choice.

The investigators may contact me in the future to ask me to take part in more research.

_____YES _____NO

What are your rights if you agree to the use of your blood/tissue for other types of research for future research?

You understand that you have the right to ask questions about any part of the future study at any time. You understand that you should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

A federal law (Genetic Information Non-Discrimination Act, GINA) will help lower the risk from health insurance or employment discrimination on the basis of genetic information. The federal law does not include other types of misuse by life insurance, long-term care or disability insurance. If you want to learn more about the GINA Law, you can find information about it on the internet or ask the study staff. In addition to the federal law, some states have laws that also help protect against genetic discrimination.

Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Therefore, your genetic information potentially could be used in ways that could cause you or your family economic stress.

There are state and federal laws that protect against genetic discrimination. A federal law, the Genetic Information Nondiscrimination Act makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: (1) health insurance companies and group health plans may not request your genetic information that we get from this research; (2) health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums; and (3) employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Authorization to use your health information for future research purposes

Because information about you and your health is personal and private, it generally cannot be used in this future research studies without your written authorization (permission). If you sign this addendum consent form, it will provide that authorization. The details of what information

we will collect and how we will use it are discussed in the main consent under the heading, "Authorization of use your health information for research purposes" near the end of the main consent document.

Also, if you authorize the use of your health information for future use, we will collect the following information about your cancer diagnosis, treatment, and outcome. And, if you agree to allow us to use your health information for future research, you are permitting us to share this information with our research collaborators at Rutgers University.

Thank you for considering participation in this research.

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

Information about you and your health is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your health information in this research study. Your information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your health information. If you sign this consent form, you agree to let the researchers use your information in the research and share it with others as described below.

What is the purpose of the research and how will my information be used?

You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help researchers answer the questions that are being asked in the research.

What information about me will be used?

If you choose to be in this study, the study doctor will get your personal and medical information. This information may include:

- All information in a medical record
- Results of physical examinations
- Medical history
- Current and past medications or therapies
- Lab tests, or certain health information indicating or relating to a particular condition as well diaries and questionnaires
- Records about study medication or drugs
- Records of blood tests
- Results of chest x-ray
- Results of imaging studies, including: MRI, CT and X-ray scans
- Information about any side effects you may experience while on study

Who may use, share or receive my information?

The research team may use or share your information collected or created for this study with the following people and institutions:

- The Rutgers Health Sciences Institutional Review Board (IRB), a group of people who review the research study to protect your rights
- Officials of the Rutgers Cancer Institute of New Jersey and
- Members of the research team, including the study doctors, research nurses and study coordinators
- Merck & Co., Inc., the company that supplies pembrolizumab for use in this study
- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Office of Human Research Protections (OHRP), involved in keeping research safe for people;
- Governmental agencies in other countries

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?

No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?

No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this research study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?

Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him of your decision:

Eugenia Girda, MD
Rutgers Cancer Institute of New Jersey
195 Little Albany Street
New Brunswick NJ 08903

How long will my permission last?

There is no set date when your permission will end. Your health information may be studies for many years.

Where can you get more information?

You may call the National Cancer Institute's Cancer Information Service at:
Voice: 1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/
For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/
If you do not have access to a personal computer, you may access these websites and other information at a computer in the Resource and Learning Center on the second floor of the Cancer Institute of New Jersey at no cost to you.

Financial Disclosure –

Dr. Salma Jabbour, a sub-investigator on this study, has a financial relationship with Merck & Co., the company that provides the study drug, Pembrolizumab (KEYTRUDA). Please feel free to ask any further questions you might have about this matter.

AGREEMENT TO PARTICIPATE

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

I agree to take part in this study.

Subject Name:_____

Subject Signature:_____ Date: _____

FOR NON-ENGLISH SPEAKING SUBJECTS:

Signature of Reader/Translator If the Subject Does Not Read English Well:

The person who has signed above, _____, does not read English well. You read English well and are fluent in _____ (*name of the language)*, a language that the subject (his/her parent(s)/legal guardian) understands well. You understand the content of this consent form and you have translated for the subject (his/her parent(s)/legal guardian) the entire content of this form. To the best of your knowledge, the subject (his/her parent(s)/legal guardian) understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered (his/her parent(s)/legal guardian).

Reader/Translator Name:_____

Reader/Translator Signature:_____ Date:_____

Witness Name:_____

Witness Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:

To the best of your ability, you have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____