

**Research Consent Form
for Biomedical Research**Dana-Farber/ Harvard Cancer Center
BIDMC/BCH/BWH/DFCI/MGH/Partners Network Affiliates

OHRS 01.08.16

Protocol Title: Phase II Trial of Pembrolizumab in Central Nervous System
Metastases from Multiple Histologies**DF/HCC Principal Research Doctor / Institution:**
Priscilla Brastianos, MD/ Massachusetts General Hospital**DF/HCC Site-Responsible Research Doctor(s) / Institution(s):**
Eudocia Kalem Quant Lee, MD, MPH / Dana Farber Cancer Institute**A. INTRODUCTION**

You are invited to take part in a clinical trial, a type of research study, because you have metastases in the central nervous system (brain and spinal cord). This research study is studying Pembrolizumab as a possible treatment for this diagnosis.

For purposes of this research, you will be referred to as a “participant.”

It is expected that about 101 people will take part in this research study.

Merck, a pharmaceutical company, is supporting this research study by providing funding for the study and study drugs.

This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational intervention to learn whether the

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intervention works in treating a specific disease. “Investigational” means that the intervention is being studied.

Pembrolizumab may help your immune system fight your cancer.

The FDA (the U.S. Food and Drug Administration) has approved pembrolizumab for some diseases that are being treated on this study, but not for central nervous system metastases. Researchers hope to study the effects of pembrolizumab. Many cancers use specific pathways (such as PD-1/PD-L1 and CTLA-4) to evade the body’s immune system. Pembrolizumab works by blocking the PD-1/PD-L1 pathways and thus releasing the brakes on the immune system so it can stop or slow cancer. In some tumor diagnoses, there may be a correlation between a specific marker (PD-L1 status) and activity of types of immunotherapies.

Researchers hope to study the effects of pembrolizumab in cancer that has metastasized to the brain. These drugs work by stimulating the immune system to fight cancer.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Receive standard treatment including: Surgery and/or Stereotactic Radiosurgery in solitary brain metastases
- Receive whole brain radiation therapy
- Receive standard chemotherapy for your metastatic cancer
- Take part in another research study.
- Receive no therapy specific to your cancer.
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms.

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

D. WHAT IS INVOLVED IN THE RESEARCH STUDY?

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Sometimes it is hard to keep track of all of the details and procedures that are part of a research study. We will describe them in this consent form and you can refer to this at any time during the research study.

Pembrolizumab will be administered every 3 weeks, with 21 consecutive days defined as a treatment cycle. The drug will be administered as an Intravenous (IV) infusion on Day 1 of each cycle.

Data Collection: Data will be collected and may be shared with an outside collaborator for analysis. The data will not be identifiable. The data will be banked for future use.

Before the research starts (screening):

After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. All screening procedures should be performed within 14 days of start of study treatment. Scans may be done within 28 days of start of study treatment. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history and demographics**, which includes questions about your health, current medications, and any allergies.
- **Review of medications**
- **A physical examination**, including a neurological assessment
- **Recording of your weight and your vital signs.** Your height will be taken at screening.
- **Performance status**, which evaluates how you are able to carry on with your usual activities.
- **Blood collection and testing**, approximately 2 tablespoons
- **Serum pregnancy test**, for women of childbearing potential
- **An assessment of your tumor** by one or more of the following standard assessment tools: CT (Computerized Tomography) scan, MRI (Magnetic Resonance Imaging) or PET (Positron Emission Tomography) scans
- **Cerebrospinal fluid** will be collected to assess disease status in some participants (those with leptomeningeal carcinomatosis) in this study. Any extra cerebrospinal fluid that is collected may be used for research. We

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will look at what makes your sample unique, and see if it can show us anything about what makes someone more or less resistant to therapies. These studies could provide suggestions as to other therapies that might help treat cancer.

Other Study Procedures

- **Dosing of the Study Drug**
- **Archival tissue collection**, which is the collection of a previously-taken biopsy of your tumor, if there is such tissue available. We will examine this data for genetic biomarkers to help identify possible biomarkers that will identify those that will respond to therapy. We will look for common mutations that could predict resistance to the therapies. These studies could provide suggestions as to other therapies that might help treat cancer. By signing this consent form, you give us permission to contact the hospital where you had any previous procedure to request a small portion of the available tissues and associated medical information such as a pathology report and treatment records. We will store these tissues and information in the same manner as in the rest of the study and seek permission to perform the same range of testing as on your tissues stored here. Whether such a tissue is shared with us will be up to the institution that is storing the tissues according to their rules or regulations.

After all routine tests required for your care are finished, instead of discarding your left over biological samples we may save them for possible future research. These tissues could include tumor tissue, normal tissue, blood, and cerebrospinal fluid.

If these tests show that you are eligible to participate in the research study, you will begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

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Research Study Plan:

	Screening	Cycles 1-8	End of Treatment	30-days Post Discontinuation
Medical History	X			
Concurrent meds	X			
Physical exam	X	X	X	X
Weight and vitals	X	X	X	X
Performance status	X	X	X	X
Blood collection and testing	X	X	X	
Serum Pregnancy Test	X			
Radiologic evaluation	X	X*		
Cerebrospinal fluid**		X		
Drug Dosing		X		

*Brain MRI and CT Chest, Abdomen, Pelvis every other cycle (every 42 days)

** Only for those with leptomeningeal carcinomatosis

In rare circumstances, we may obtain a sample outside of a routine medical procedure. If this happens, you will be clearly informed at the time we would like to collect these and will be able to decide whether or not you would like to undergo the procedures (e.g. drawing blood) to provide these samples. When you are approached for this additional sample you can decide you do not want any additional procedures done to obtain these samples and it will not affect your participation in this study.

Planned Follow-up:

After documented disease progression, you will be followed by telephone. Every 6 weeks after discontinuation and then every 3 months after, the status of your disease and your health will be collected.

E. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for as long as you are responding to and tolerating treatment.

The research doctor may decide to take you off the research study for many reasons including if:

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- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- Your condition worsens
- A decision is made to close the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

If you are removed from the research study, the research doctor will explain to you why you were removed.

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study. If you decide to stop participating in this research study, we encourage you to talk to the research doctor and your primary doctor first.

F. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. Some side effects can be mild; but others can be long lasting and may never go away. Some may be life-threatening or fatal.

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you

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are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

Risks Associated with Pembrolizumab:**Very Common: (Greater than a 10% chance that this will happen)**

- Feeling tired, lack of energy. Rarely, this could be severe and make it difficult to perform daily activities.
- Frequent or less often than usual bowel movements
- Rash or itching of the skin
- Pain in a joint
- Nausea
- Fevers

Common: (Between a 2-10% chance that this will happen)

- Cough that may or may not bring up mucous
- Headache
- Pain or cramping in a muscle or group of muscles
- Loss of appetite
- Loss of skin color
- Low thyroid function which may cause you to feel tired, weight gain, or feel cold easily
- Increased release of thyroid hormone, which may manifest as: anxiety, irritability, or trouble sleeping, weakness, trembling, sweating, feeling uncomfortable in warm weather, fast or uneven heartbeats, feeling tired, weight loss, and frequent or excessive bowel movements.
- Shortness of breath while at rest or while performing physical activity.
- Feeling cold
- Abnormal laboratory result of liver test by blood that occasionally indicates liver failure, manifesting as yellowing of the skin or whites of the eyes, fatigue, or leg swelling
- Vomiting.

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- Inflammation of the lungs, manifesting as shortness of breath and difficulty breathing, particularly if you have cancer in your lungs. Inflammation of your eyes
- Cerebral Edema, which is swelling in the brain. This can cause headache, dizziness, nausea, numbness or weakness, loss of coordination or balance, loss of the ability to see or speak, seizures, lethargy, memory loss, and/or altered level of consciousness
- Arthritis, which is swelling of the joints
- In some tumor diagnoses, there may be a correlation between a specific marker (PD-L1 status) and activity of types of immunotherapies.
- Joint pain
- Pain in your belly
- Low levels 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: (Less than a 5% chance that this will happen)

- 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, experience a decrease in your blood pressure 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: (Less than a 1% chance that this will happen)

- Severe skin, stomach lining, and digestive tract reaction that may include rash and sloughing or breakdown of tissue. This may manifest as various

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- blisters, hives, and other lesions in various locations on the body including palms and soles, face and other extremities. This is serious and may be life threatening.
- Inflammation of the heart muscle, usually caused by infection. May be serious and require hospitalization.
 - Inflammation of the kidneys. This may have the following symptoms: swelling of the body, change in urine output, changes in blood pressure, rash and fatigue
 - Inflammation of the pituitary gland. This can cause headaches, weakness, dizziness and vision changes.
 - Inflammation of the pancreas. This can cause nausea, vomiting and abdominal pain.
 - Multi-organ disease causing lesions, most often in the lungs
 - Muscle weakness
 - Brain Inflammation (possible paralysis and/or coma)
 - Inflammation of the nerves that may cause pain, weakness, or tingling in 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 pain in the top part of your belly 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 redness, blurred vision, sensitivity to light, 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, a pain in the right side of 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 kidney) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle and bellyaches, nausea, vomiting, loose or watery stools, 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 insulin shots

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- 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, difficult 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.
- Low levels of parathyroid hormone (a hormone made by 4 tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling or burning in your fingertips, toes or lips (hypoparathyroidism)

Additionally, since pembrolizumab was approved, the following side effects have been reported by people receiving pembrolizumab. It is not possible to estimate the frequency of these side effects:

- 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)

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- 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 the right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis)
- Inflammation or swelling of the nerve fibers of the eye which send visual information from your eye to your brain. This health condition often has a sudden onset of vision loss, loss of color vision, pain when moving your eyes, and/or loss of peripheral vision. It may affect one or both eyes at the same time (optic neuritis)

Some drug reactions can rarely be fatal and may occur even after discontinuation of pembrolizumab therapy.

Radiation Risks Associated with Scans and X-Rays:

While you are in this research study, CT scans and/or other scans utilizing radioactivity may be used to evaluate your disease. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

Risks Associated with Stereotactic Radiosurgery (applies to Cohort D of the study):

Stereotactic radiosurgery (SRS) refers to the delivery of high dose of radiation in a single treatment by using a highly accurate and reproducible three-dimensional coordinate system for localization. Several stereotactic systems exist to achieve submillimeter precision. At the Massachusetts General Hospital, immobilization is achieved by using a stereotactic frame that incorporates a bite piece that relies on the uniqueness of one's dental impression. In some cases, fiducial markers in the form of metal ball bearings may be implanted in the bone of the outer skull in order to assist with confirming correct position immediately prior to the radiation treatment. The treatment itself occurs as an outpatient several days later and typically requires about one hour. You will be lying on a table wearing the stereotactic frame. The treatment machine will rotate around you stopping at the positions that were designed for your specific treatment. During treatment, you should not feel anything. Depending on the location of your tumor(s), your physician may prescribe you medications to prevent seizures.

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As noted below, stereotactic radiosurgery can lead to injury to the small amounts of brain that are treated. In the vast majority of occurrences, this injury can be seen by MRI but remain asymptomatic. Rarely, they can produce neurologic symptoms which are dependent on the location within the brain. These changes may occur within months or even years later. In cases of multiple brain metastases treated with stereotactic radiosurgery, each treated tumor may carry this risk independently.

Common: (More than 10% chance that this will happen)

- Small areas of hair loss
- Injury or inflammation to the treated brain tissue that can be seen by MRI but remains asymptomatic

Uncommon: (Less than 10% chance that this will happen)

- Fatigue
- Nausea and vomiting
- Headache
- Seizures
- Injury or inflammation to the treated brain tissue that leads to neurologic symptoms depending on its location
- Inflammation of a blood vessel or blood vessels
- Infection of the liver's bile ducts

Reproductive Risks:

The drugs used in this research study may affect a fetus. While participating in this research study, you should not become pregnant or father a baby, and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

In the event that your partner becomes pregnant, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy.

Non-Physical Risks:

Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

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G. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

Taking part in this study may or may not help you because researchers do not know how Pembrolizumab will compare to the usual approach. This study may help researchers learn things that may help people in the future.

H. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the study drug(s). In some cases, the abrupt stopping of a drug can have risks in itself. Another reason to tell your research doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

I. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid to participate on this study. We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

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You will not be charged for Pembrolizumab. It is possible that Pembrolizumab may not continue to be supplied free for some reason. If this would occur, your research doctor will talk with you about your options.

You or your insurance company will be charged for portions of your care during this research study that are considered standard care. You may be responsible for co-payments and deductibles that are typical for your insurance coverage.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services is:

- Brigham and Women's Hospital: (617) 732-5524 or (617) 732-7485
- Dana-Farber Cancer Institute: (617) 632-3455
- Massachusetts General Hospital: (617) 726-2191

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF I AM INJURED OR SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. The treating hospital may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for any of the sponsors of this study to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

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L. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database. The results of this research study may be published. You will not be identified in publications without your permission.

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.

As part of this study, your de-identified specimens, MRI scans, or genetic data may be placed into one or more publicly-accessible scientific databases, such as the National Institutes of Health's Database for Genotypes and Phenotypes (dbGaP). Through such databases, researchers from around the world will have access to de-identified samples or data for future research.

M. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Massachusetts General Hospital

- Priscilla Brastianos, MD: (617)-643-1938

Dana Farber Cancer Institute

- Eudocia Kalem Quant Lee, MD, MPH: (617) 632-2166

24-hour contact: Please call MGH at (617) 724-4000 and ask that the study doctor be paged.

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at DFCI (617) 632-3029. This can include questions about your participation in the study, concerns

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about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

N. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions (“protected health information”). If you enroll in this research study, your “protected health information” will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug for the purpose of this or other research relating the study drug and its use in cancer; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

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3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor of the study, its subcontractors, and its agent(s): DF/HCC
- The funder (s) of the study, its subcontractors, and its agent(s): Merck
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

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5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

O. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study may be stored and used for future research. If so, any personal identifiers will be removed so that the information or samples cannot be linked back to you. As a result, we will no longer be able to identify and destroy them.

Investigators, including investigators from collaborating institutions, can request this data and samples for new research. Samples and data may also be shared with outside non-profit academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate.

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You will not be asked to provide additional informed consent for the use of your de-identified information or samples in future research.

Future research studies may include genetic research. Your genes are unique to you. At this time, you cannot be identified through this research. There is a risk that you might be reidentified in the future as genetic research progresses.

P. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant
or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

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Adult Participants

To be completed by person obtaining consent:

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

- ☐ A copy of this signed consent form will be given to the participant or legally authorized representative, or, where the participant is a minor, the participant's parent or legal guardian.

For Adult Participants

- ☐ 1) The participant is an adult and provided consent to participate.

- ☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

- ☐ 1b) Participant is illiterate

The consent form was read to the participant who was given the opportunity to ask questions.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

- ☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ 2a) gave permission for the adult participant to participate

- ☐ 2b) did not give permission for the adult participant to participate

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