Informed Consent Form

RAD3179-16: Pilot Study of Pembrolizumab and Stereotactic Radiation Surgery (SRS) for Patients with Melanoma or Non-Small Cell Lung Cancer (NSCLC) Brain Metastases (BM)

NCT Number: NCT02858869

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You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

EMORY UNIVERSITY | Institutional Review Board
Research Administration

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: Rad3179-16 (MK-3475-423) Pilot Study of Pembrolizumab and Stereotactic Radiation Surgery for Patients with Melanoma or Non-Small Cell Lung Cancer Brain Metastases

Lay title: Testing the safety of combination of radiation and drug, pembrolizumab, for melanoma and non-small cell lung cancer that has spread to the brain.

Principal Investigator: Mohammad K. Khan, MD, PhD

Sponsor: Mohammad K. Khan, MD, PhD

Study Supporter: Merck Sharp & Dohme Corp.

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?

You are being asked to take part in this medical research study because you have melanoma or non-small cell lung cancer that has spread to the brain. People who are not in a study are usually treated first with stereotactic radiotherapy (a technology that focuses high-dose radiation upon a desired target); weeks later, they are then treated with any chemotherapy that is FDA approved. For both melanoma and non-small cell lung cancer patients, this chemotherapy after radiation may include the FDA approved study drug, pembrolizumab.

Receiving stereotactic radiotherapy and the study drug, pembrolizumab, at the same time is not FDA approved yet and therefore the study is considered investigational.

The length of study participation including treatment with pembrolizumab is about 2 years or until your disease gets worse (progress).

How is this different from the standard of care?
This study is different from the standard of care because it gives pembrolizumab and stereotactic radiosurgery at nearly the same time. This may or may not increase the side effects and/or the response to each of the therapies.

How many people will take part in the study?
A maximum of 40 people will be in the study.

What are the study groups?
All patients will receive the study drug, pembrolizumab. Within 1-2 days after the first treatment with the drug, your disease in the brain will be treated with radiation. This study then has three groups, based on the radiation treatment.

Different groups on this study will receive different doses of the stereotactic radiation. All three radiation doses are considered reasonable radiation dosing regimens by your doctors. There are good institutional series that support all three radiation doses as being safe. The first 6 patients will be enrolled on each of the three different radiation dose arms. This will be followed by a waiting period, to assess for safety. Once safety is assessed, another 6 patients will be enrolled. If any radiation dose arm does not meet the safety criteria, enrollment on that radiation dose arm will be stopped.

What will I be asked to do?
If you take part in the study, you will need to do the following:

- Visit the study doctor as instructed. Each study therapy cycle is about 3 weeks. The study doctor or staff will discuss with you when and on which days to report to the clinic.

- If you agree to take part in this study, it is very important that you tell your study doctor before starting on this study about all of the medicines you are taking or have recently taken (over-the-counter medications, supplements, prescription medications, or recreational drugs). The reason this is important is that some medicines can change the way your body handles other medicines and this can increase the risk of side effects from the study drug. In addition, please talk with the study doctor before you begin taking any new medications or supplements during this study. Your study doctor will look at the medicines you are currently taking to make sure you are allowed to take them while on the study. You may be asked to change some of the medicines you are taking. If you need to take a medicine that is not allowed and it cannot be replaced with another medicine, you will not be asked to stop taking it; however, if you can't stop taking it, you will not be able to take part in this study.

- If your blood tests show that you have liver lab results that are not normal, the study doctor or staff will ask you to provide additional samples of blood for testing to find out why your liver lab results are not normal. If you do decide to provide the samples, the study staff will discuss with you the amount of the additional samples of blood that will be taken and the tests that will be performed on the blood.

- The tests that may be performed include HIV and viral hepatitis tests to find out if HIV or hepatitis is the reason your liver lab results are not normal. Depending on the region where you live, you may need to sign another consent form to have these tests done.

- The results of all of your blood tests, just like all other laboratory test results, will be provided to the Sponsor (the company, department, or person who is paying for the medical research study). Positive HIV and Viral Hepatitis test results will be reported to local health authorities according to local laws. You will be notified of the results and provided appropriate counseling, if the results are positive. Your spouse and/or sexual partner may also undergo appropriate counseling.

- If you have visible skin disease, you will be asked to provide a biopsy from this site previous to starting treatment and after completing therapy. This is optional and not required. Your tumor samples may also be used for the analysis of additional biomarkers (a substance or activity that can be measured and serves as a marker of a specific biological activity) to investigate ways that the study drug does or does not work to shrink tumors. Other additional biomarkers which may impact how individuals respond to the study drug may also be analyzed. These results are for research only. Since these tests are exploratory research only, they will have no clear implications about you or your family's medical conditions. The results of the testing will not be returned to you.

- You will be asked to provide blood samples to be used for studying biomarkers in the blood. These samples will be used to analyze biomarkers to discover ways that the study drug does or does not work to shrink tumors. Additional biomarkers which may impact how individuals respond to the study drug may also be analyzed. Any sample left over will be destroyed once all study related needs have been met. Your sample will not be saved for future testing. The results of the testing will not be returned to you.

- It is your decision whether you provide the additional samples and have these tests performed. However, if you decide not to provide the additional samples and have the tests done, you may need to leave the study for your own safety (as the cause of your abnormal liver lab results may not be able to be determined without them).

- Take study drug (pembrolizumab) as instructed (study drug is administered by infusion into one of your veins).

    - Pembrolizumab (MK-3475) will be given as a 200 mg IV dose on first Day 1 of every 3–week treatment cycle. There will be 4 treatment cycles for a total of 4 cycles.
    - The time between doses of pembrolizumab will be approximately every 21 days (3 weeks). The time between doses may increase if you experience bad side effects.

- Receive stereotactic radiosurgery radiation (SRS) as delivered by the radiation oncologist.
    - Stereotactic radiosurgery will be delivered on days 2-3. Depending on which dose level you are assigned, you may receive 1 single treatment, 3 treatments, or 5 treatments per standard of care. For patients planned to receive multiple treatments, each treatment will be delivered at least 40 hours apart. All radiation treatments will be finished by week 2, day 14.

- Receive supportive care for symptoms or adverse effects from therapy. This includes, but is not limited to, steroids, anti-diarrhea medications (e.g. loperamide, atropine), anti-nausea medications (e.g. promethazine, prochlorazine, ondasetron), and anti-seizure medications (e.g. levetiracetam).

Ending Study Drug:

You will take the study drug as long as your cancer does not get worse over two years or until you disease get worse (progress).

Safety and Survival Follow-up:
You will be followed for at least 30 days after the last dose of study drug or until you start a new cancer treatment, whichever happens first.

You will be asked to complete the 30-day follow-up visit and then you will enter the post-treatment follow-up period. The study doctor or staff will discuss with you when and on which days to report to the clinic for the follow-up visits.

If you stop taking the study drug before your cancer gets worse (disease progression) you will continue to come in for a follow-up visit every 12 weeks to monitor your disease status and to perform additional study related testing (which also may include blood sample collections and tumor imaging) until your cancer gets worse or you start a new treatment for your cancer.

If at any time during post-study drug treatment your cancer gets worse, or you start a new cancer treatment, you will be contacted by telephone about every 12 weeks for survival follow-up until the study ends.

What will happen during the study visits?
When you come in for your study visits, the study doctor or staff may do any or all of the following to measure if the drug is working and/or to monitor your health.

- Give you a subject ID card.
- Administer study drug.
- Review your medical history and health.
- Review the medications you have taken and your current medications.
- Perform a physical exam.
- Collect your vital signs (including your temperature, pulse, breathing rate, and blood pressure).
- Measure your height and weight.
- Collect blood and urine samples:
    - For safety tests.
    - For biomarkers study
    - To perform a pregnancy test if you are a woman able to have children.
- Perform a CT scan, MRI, PET scan, or x-ray of your tumor. A Brain MRI will also be performed to verify that there are detectable brain metastases.
- Assess your disease status and ability to perform physical tasks.
- Review any side effects you have had.
- Optional Skin Biopsy for Melanoma patients at the screening pre-treatment phase

What is the expected schedule of events?

Event	Day of Event
Initial Evaluation	up to 28 days before stating on the protocol
History, Physical	up to 28 days before stating on the protocol
Scans (including Brain MRI, CT chest/abdomen/pelvis, PET scan)	up to 28 days before stating on the protocol
Lab work	up to 28 days before stating on the protocol

Radiation treatment planning (CT simulation & MRI Brain)	(within 1-2 weeks before starting on the protocol)
Drug Treatment #1	Day 1
Radiation Treatment #1	Day 2 or Day 3
Radiation Treatment #2	Between Day 4 - Day 7 (one of these days only)
Radiation Treatment #3	Day 7-8 (one of these days only)
Physical Exam, Review of symptoms and side effects	Day 7-8 (on same day as radiation)
Radiation Treatment #4	Day 8-9 (one of these days only)
Radiation Treatment #5	Day 10-13 (one of these days only)
Physical Exam, Review of symptoms and side effects	Day 22
Labs	Day 22
Drug Treatment #2	Day 22
Physical Exam, Review of symptoms and side effects	Day 43
Labs	Day 43
Drug Treatment #3	Day 43
Physical Exam, Review of symptoms and side effects	Day 64
Labs	Day 64
Drug Treatment #4	Day 64
Physical Exam, Review of symptoms and side effects	Day 91
Labs	Day 91
Scans (including Brain MRI, CT chest/abdomen/pelvis, PET scan)	Day 91
Physical Exam, Review of symptoms and side effects	Every 3 months after day 91
Labs	Every 3 months after day 91
Scans (including Brain MRI, CT chest/abdomen/pelvis, PET scan)	Every 3 months after day 91

What extra test and procedure will I have to take part in the study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra *tests* that you will need to have if you take part in this study. These include:

- Receiving multiple fractions of radiation therapy instead of potentially receiving a single fraction or treatment.
- You may be asked to have blood drawn more frequently, especially during the first week.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

Who owns my study information and samples?
If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

You will not be able to request destruction of your samples that were already collected for this study.

What are the possible risks and discomforts?
You may feel discomfort during some of these tests or may experience some inconveniences. Some may also have risks, which may include:

- **Blood samples:** drawing blood from your arm may cause pain, bruising, lightheadedness, and rarely, infection.
- **IV line**: may cause discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely, infection, nausea, and lightheadedness. Because pembrolizumab is an antibody, there is the possibility that you may experience an acute infusion reaction. These are side effects that develop during or immediately after the administration of pembrolizumab. Signs and symptoms may include:
  - Blood pressure changes (increase or decrease)
  - Cough
  - Dizziness
  - Fast heart beat
  - Feeling cold
  - Feeling that the tongue is swelling or your airway is closing and you have trouble breathing
  - Fever
  - Headache
  - Joint pains
  - Muscle pains
  - Nausea
  - Rash, hives, or itching
  - Shortness of breath
  - Sweating
  - Tiredness
  - Vomiting

- **Magnetic Resonance Imaging (MRI)**: Risks of MRI include claustrophobia, discomfort due to lying still for a prolonged period of time, and other factors which will be described to you and discussed with you at the MRI center.

- **PET Scan**: PET scan side effects are not common, and when encountered are usually mild, such as nausea and vomiting, or you may become uncomfortable lying still for the duration of the examination. The PET scan involves an injection, in the vein of your arm, of a radiotracer (radioactive compound that localizes in the areas that are active). The injection of the radiotracer may feel like a small sting and there may be possible bruising at the injection site. .

- **Tumor Biopsy**: Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy, shortness of breath from lung collapse and rarely, death. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. Other potential risks will be described to you and discussed with you by physicians who conduct these biopsies.

- **Radiation Pneumonitis:** Pembrolizumab can lead to pneumonitis (inflammation of the lung, shortness of breath, cough, etc) in small subset of patients. If you have a history of (non-infectious) pneumonitis that required steroids or current pneumonitis, you will not be eligible for this study. Please notify your doctor.

- **Study Drug: 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.

  Overall, as of 03-Mar-2018, approximately 25,519 patients have been treated with pembrolizumab in clinical studies.

  Pembrolizumab works by helping your immune system to fight your cancer.

  However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab.

  What side effects could the study drug(s) cause?
  VERY COMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life- threatening or where noted, may cause death)
  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, SOME MAYBE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)
  Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

  - Joint pain
  - Rash
  - Fever
  - Back pain

- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach

UNCOMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life- threatening, or where noted, may cause death)
Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs so you may feel short of breath and cough. Sometimes this might lead to death
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools
- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or 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
- 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. These severe conditions can sometimes lead to death.

RARE, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)

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 in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the muscles so you may feel weak or have pain in your muscles
- 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 vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- 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 of your belly, yellow eyes and skin, and dark urine
- 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
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- 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
- 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. Sometimes this condition can lead to death
- 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.
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs
- 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.
- Generalized lipodystrophy which is widespread loss or lack of adipose (fat) tissue leading to muscle weakness, abnormal gait, and impairment in brain function (difficulty speaking, or disorientation).
- Myelitis is inflammation of the spinal cord which can disrupt the normal responses from the brain to the rest of the body, and from the rest of the body to the brain. This can lead to changes in sensation or weakness or loss of movement in some parts of the body.
- Vogt-Koyanagi-Harada syndrome is a multisystem inflammatory disorder characterized by visual changes, and it is often associated with changes in skin color cutaneous manifestations, including headache, and hearing loss.

Additionally, since pembrolizumab 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

In addition to the above, 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 receives 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 (cancers 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.

Are there any other risks?
There may be other side effects or risks that are not known at this time.

Are there pregnancy risks?
Female:
It is not known if the study drug(s) may affect an unborn or nursing baby. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a blood or urine pregnancy test before the start of and during the study, if you are able to have a baby.

If you are able to have a baby, you must use an adequate birth control method or abstinence (not have sex) for the duration of the study and for a period of 120 days after your last dose of pembrolizumab.

If you become pregnant during the study you must notify the study doctor right away. The study drug will be stopped and you will be taken out of the study.

Male:
There may be risks if you are male and your partner is pregnant or trying to become pregnant. If you are male and your partner is able to have a baby, you and your partner must use an adequate birth control method or abstinence for the duration of the study and for a period of 120 days after your last dose of study drug pembrolizumab.

If your partner becomes pregnant during the study you must notify the study doctor right away. If your partner is already pregnant when you begin the study you must use an adequate birth control method or abstinence for the duration of the study and for a period of 120 days after your last dose of pembrolizumab. You must also agree to not donate sperm during the study and for a period of 120 days after your last dose of study drug.

If you will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

About The Radiation Treatment

What is known about this study radiation treatment?
Stereotactic radiation therapy is a form of radiation that is delivered only to places in the brain that have a tumor(s). Areas of the brain that do not have cancer will receive minimal radiation. On this study, you

will receive one of 3-radiation doses. These doses have been used before and have similar ability to control tumors. There are institutional series to support all three radiation doses as reasonably acceptable.

What side effects could the radiation cause?
The study doctor believes that the following side effects may be caused by stereotactic radiation therapy. However, these are considered to part of your standard of care side effects.

Very common side effects seen in at least 20% of patients treated with stereotactic radiation therapy include the following:
Right away (during treatment or up to 1-2 months afterwards):
- Fatigue
- Temporary hair thinning or hair loss
- Skin irritation and/or tanning
- Headache
- Tumor Swelling

Delayed (month to years after treatment):
- Increased risk of cataract development (less likely with radiosurgery).

Common side effects seen in >10% of patients treated with stereotactic radiation therapy include the following:
Right away (during treatment or up to 1-2 months afterwards):
- Nausea
- Vomiting
- Eye irritation
- Nasal congestion
- Ear fullness

Months to years after treatment:
- Radiation necrosis or dead tissue from treating the tumor built up in the brain
- Short-term memory loss

Severe side effects seen in 1% to 4% of patients treated with stereotactic radiation therapy include the following:
Right away (during treatment or up to 1-2 months afterwards):
- Seizure
- Bleeding in the tumor
- Stroke like symptoms from bleeding into tumor

Months to years after treatment:
- Neurologic damage
- Vision loss
- Stroke like symptoms
- Seizure

Are there other risks from radiation therapy?
If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you

have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you are a man: the effect of radiation on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant while receiving radiation and for 6 months after the last dose. You and the study doctor should agree on a method of birth control to use throughout the study.

In addition to radiation therapy, you may receive additional radiation from diagnostic procedures to evaluate your condition. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. However, the additional risk of radiation-induced cancer from these diagnostic procedures is low compared to the risks from radiation therapy.

What are the risks of having combination therapy of Pembrolizumab and Stereotactic Radiation Therapy?

Receiving both therapies at the same time may or may not increase the side effects and/or the response to each of the therapies, as described in the above sections.

Are there any other points to know about side effects?

Yes. They include:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death

Will I benefit directly from the study?

It is not possible to know at this time whether or not the study treatments will help you. The drug has shown benefit in patients with melanoma and non-small lung cancer, but it is unknown if this applies to patients whose disease has spread to the brain. Also, it is unknown if giving radiation and the drug close together will help or hurt. If the combination therapy works, you may have some benefit. If the combination does not work or produces too many side effects, you may not benefit.

This study may help us learn things that may help people in the future. The Sponsor does not intend to provide you with ownership or financial benefits that may result from this study.

Will I be compensated for my time and effort?

You will not be offered payment for being in this study.

What are my other options?

If you should decide not to participate in, or if you withdraw from this study, the study doctor can recommend other treatments.

Alternative treatments for your cancer include

- A marketed drug or treatment with a different study drug
- Radiation therapy treatments alone, including stereotactic radiosurgery or whole brain radiation therapy.

- If you decide you don't want any more active treatment, one of your options is "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

If you have questions about alternate treatments and their potential benefits and risks, ask the study doctor for additional information. **You do not need to participate in this study to be treated for your advanced cancer by your physician.**

How will you protect my private information that you collect in this study?
Emory will keep any research records that it creates private to the extent that this is required to do so by law. Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Medical Record
If you have been an Emory Hospital patient before, then you already have an Emory medical record. If you have never been an Emory patient, you do not have one. An Emory and medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory medical record you have now or any time during the study.

What Happens In Case of Injury?
If you get ill or injured from being in the study, Emory will help you get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Mohammad Khan at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

What are the costs of being in the study?
The study sponsor will pay for certain items and services that you may receive if you take part in this study.

Study sponsor will pay for pembrolizumab and will not pay for Stereotactic Radiation Therapy.

You will have to pay for the items or services for which the study sponsor does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory will submit claims to your insurance for items and services that the sponsor does not cover. Emory will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay

for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

Your decision to participate in this study is voluntary (your decision). You can choose at any time to withdraw (end participation) from the study by telling the study doctor without any penalty or loss of benefits to which you are entitled. If you choose to stop taking the study drug, please tell the study doctor/staff so this can be done safely. If at some point you consider withdrawing from the study, you can decide if you are willing to continue to provide information or not. This would be helpful for the purposes of the study. To help you decide, the study doctor/staff can tell you which study procedures and information collection would still apply if you stop taking the study drug but choose to remain in the study.

The researchers and Merck also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest
- You were to object to any future changes that may be made in the study plan
- Reasons specific to this study
- Or for any other reason

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study and for any optional studies in which you may choose to participate.

Main Study

PHI that Will be Used/Disclosed:

The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:

We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such

treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Mohammad Khan, MD, PhD is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration;
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Merck Sharp & Dohme Corp., the study supporter and manufacturer of the study drug
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Optional Study: Skin Biopsy for Melanoma patients at the screening pre-treatment phase

PHI That Will be Used/Disclosed for Optional Study:
The PHI that we will use and/or disclose (share) for the optional research study includes:

- Dates of medical procedures
- Any diagnosis and stage of your disease (if you have cancer)
- Your age and race
- Medical and family history
- Treatments you had
- How you responded to treatments

Purposes for which your PHI will be Used/Disclosed for Optional Study:
We will use and disclose your PHI for the conduct and oversight of the optional storage and future research use of your PHI.

Authorization for This Use of PHI is Required to Participate in Optional Study, but Not in Main Study:
You do not have to authorize the use and disclosure of your PHI. If you do not authorize the use and disclosure of your PHI for the optional study, then you may not participate in the optional research study. You can still be in the main research study even if you don't participate in the optional study.

People Who Will Use/Disclose Your PHI for Optional Study:
The same people and groups who will use and disclose your PHI for the Main Study will also do so in connection with the optional research study/storage of PHI for future research.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Dr. Mohammad Khan, MD, PhD
Winship Cancer Institute, Emory University
1365 Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will

have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Mohammad Khan at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

Optional Study

□ **Not Applicable**

Please circle and initial your answers to show whether or not you would like to take part in each option and let your PHI be used and disclosed as described for the sub-studies:

SKIN BIOPSY SAMPLES for Melanoma patients:

I agree to have my skin tissue specimen collected and I agree that my specimen sample(s) and related information may be used for biomarker study.

YES _____Initials NO _____Initials

This is the end of the section about optional studies.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ am / pm
Signature of Subject (18 or older and able to consent) Date Time (please circle)

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm
Signature of Subject (18 or older and able to consent) Date Time (please circle)