UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title: **Imaging the flare response with FDG PET/CT in patients with advanced metastatic melanoma on pembrolizumab.**

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Why am I being asked to volunteer?

You are being invited to participate in a research study because you have been diagnosed with melanoma. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the

possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

The purpose of this study is to learn more about how melanoma responds to pembrolizumab, a therapy designed to boost your immune system. Measuring how melanoma responds to pembrolizumab can be difficult with standard imaging, such as CT scans and MRI, especially when the imaging is performed early in the course of therapy. In this study, we will use an imaging method called Positron Emission Tomography / Computed Tomography (PET/CT) to determine if your melanoma tumors are responding to treatment within the first few weeks of starting pembrolizumab. We will also collect additional biopsy tissue and blood samples to study markers of immune response after pembrolizumab.

How long will I be in the study? How many other people will be in the study?

Up to 35 patients with advanced melanoma will take part in this study. If you choose to participate in this study you will have a baseline FDG PET/CT scan before starting pembrolizumab and a 2nd FDG PET/CT scan approximately 1 week after starting pembrolizumab. In some cases the baseline FDG PET/CT may be done as part of your standard care. After more than 10 weeks of pembrolizumab, a 3rd imaging study will be done as part of your standard care; the 3rd imaging study may be done using FDG PET/CT, MRI or CT imaging. After completion of the 3rd imaging study your active participation in this study will be completed. After your active participation is completed we will continue to follow your medical records to collect information about your treatment as long as you are undergoing care for melanoma.

What am I being asked to do?

FDG PET/CT scans

In Nuclear Medicine scans, imaging is done with specialized cameras that can pick up the tiny radiation signals given off by a radioactive tracer and determine where the signals come from. In this way, we can form a picture of where the tracer goes after it is injected. If you agree to participate in this research, the type of scan we will perform is called a Positron Emission Tomography (PET/CT)

scan, which uses a large doughnut shaped detection device to provide a map of where tracers go.

The tracer used for this study is called [^{18}F]fluorodeoxyglucose (FDG). FDG is a specialized radioactive PET tracer used to see how tumors use glucose, a sugar. FDG is an FDA-approved radiotracer that is commonly used to detect and monitor response in different types of cancer. FDG PET/CT scans are frequently used in normal clinical care to measure the spread of cancer and to evaluate how the cancer responds to treatment. **In this study you will have up to two (2) additional FDG PET/CT scans performed at the University of Pennsylvania**:

1) A baseline scan (FDG 1) before starting pembrolizumab will be done for the purpose of this study. In some cases the baseline FDG PET/CT may be done as part of your standard care.
2) A second scan (FDG 2) done after approximately 1 week of treatment, which will be done only for the purpose of this study.
3) A third scan (FDG 3) done after more than 10 weeks of treatment. This scan will be ordered by your physician as a standard part of your clinical care. In some cases MRI or CT imaging may be used instead of FDG PET/CT.

Each FDG PET/CT scan will require up to 2 hours of your time. The scan will take place using one of our PET/CT scanners in the Perelman Center for Advanced Medicine or the Hospital of the University of Pennsylvania. An intravenous (IV) line will be inserted into a vein in your arm or hand. A small amount of blood (less than one teaspoon) will be drawn from the IV to test your blood sugar. The FDG tracer will be injected using the IV and then flushed with normal saline (salt water). You will be asked to rest in a quiet room and limit activity for about one hour. You will be asked to go to the bathroom and remove any metal objects before entering the scanner. You will lie face up on a comfortable table for up to an hour, while the PET/CT machine collects imaging information.

Blood Draws

You may have already chosen to participate in another study called the Penn Melanoma Tissue Collection Program (UPCC #08607, IRB #703001). If you are already participating in this program then blood samples will be collected after you start pembrolizumab at 0, 3, 6, 9, 12, 15 weeks and at 1 year. For the purposes of this imaging study we will add one additional blood sample 1 week after you start pembrolizumab. If you have not agreed to participate in the Penn Melanoma Tissue Collection Program, then no blood samples will be drawn for the purposes of this study.

Tumor Biopsy

You may have already chosen to participate in another study called the Penn Melanoma Tissue Collection Program (UPCC #08607, IRB #703001). If you are already participating in this program then you may already have undergone or

will undergo a tumor biopsy as part of your clinical care before you start pembrolizumab. For the purposes of this imaging study we will add another tumor biopsy that will be performed within 7 days after the 2nd FDG PET/CT scan. If you agree to the additional biopsy then a Punch Biopsy (a small round piece of skin, usually the size of a pencil, is obtained using a sharp, hollow instrument); or Fine Needle Aspirate (FNA)(a small, fine-gauge needle is inserted into the area and the needle is rocked gently to obtain as much tissue as possible); or Core Needle Biopsy (CNB)(much like an FNA, a slightly larger, hollow needle is used to withdraw small cylinders (cores) of tissue from the abnormal area, will be performed for research purposes only. Research tests that are done on the tissue collected will be used for study purposes only and will not be part of your clinical medical record or used to make decisions about your clinical treatment.

You will also be asked to give permission for us to get access to biopsy tissue that has been collected as part of your standard clinical care or as part of the Penn Melanoma Tissue Collection Program.

If you have not agreed to participate in the Penn Melanoma Tissue Collection Program, then no tumor biopsies will be done for the purposes of this study.

You will be asked to return for standard clinic visits with your oncologist at normal intervals for the therapy that you receive; all procedures performed at your clinic visits will be standard of care. This may include a physical exam, vital signs, blood tests and other imaging scans. Information from these visits will be collected from your medical records for the study. You may be contacted by phone if additional information is needed.

What are the possible risks or discomforts?

You may have side effects while on the study. Everyone taking part in this imaging study will be watched carefully for any side effects.

You should talk to your study doctor about any side effects that you believe are related to the imaging procedures.

FDG PET/CT scans

During the PET/CT scan procedure, you will be required to lie quietly and motionless while the camera collects imaging information. This may cause you to experience discomfort or musculoskeletal pain (such as back or neck pain). Some people do not like the small space (claustrophobia) and might feel confined or bothered by being in the PET/CT scan machine. If you are someone who experiences claustrophobia, your physician may opt to prescribe a medication to relax you during the scans.

This research study involves exposure to radiation from an FDG PET/CT. Therefore, you will receive a radiation dose. You may have some or all of these procedures even if you do not participate in this study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

There may be unknown risks with FDG PET/CT scans. Additionally, all drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening.

An intravenous catheter will be placed into a vein in your arm or hand. Insertion of the needle may cause pain or a stinging sensation, bruising, bleeding, a blood clot, or infection at the site of insertion. Standard precautions will be taken to try to prevent any of this from happening.

You will not be able to participate in this study if you are pregnant or breast-feeding due to the risks to the fetus or child from radiation exposure. If you are a woman of child-bearing potential you will be asked to have a blood or urine test at screening to test for pregnancy. In addition, at the time of each FDG PET/CT scan you will be asked if you might be pregnant. If you are unsure, then you will be asked to provide a urine sample to test for pregnancy. If you are pregnant, you will not undergo the FDG PET/CT scan.

If you become pregnant during this study please notify the study investigator or staff. You will be taken off the study and will not undergo any further FDG PET/CT scans.

Biopsy related risks

Risks of using stored tissue:
For your “archived” tissue blocks, we will follow the institution’s standard procedures for patient protection and releasing the archived tissue for research when we request release of tissue for this study. We will make all efforts to avoid having the removal of blocks/tissue have any effect on your future clinical care. However, there is the potential risk that the entire stored sample may be used up and therefore may not be available for future clinical assessments as part of your routine care.

Punch biopsy and Core needle biopsy:
The possible risks of Punch biopsy and Core needle biopsy may include pain, discomfort, soreness, redness, swelling, bleeding, bruising, drainage from the biopsy site, abnormal wound healing, scar, fever, infection and allergic reaction to the medication that is used to numb the skin over the biopsy site.

Fine needle aspirate:
The possible risks of Fine needle aspirate may include pain, discomfort, soreness, bleeding, bruising, swelling and infection at the needle insertion site.

Blood Draws
In most cases we will add research blood tubes to your clinical labs, in some cases if a research specific blood draw is needed trained personnel will obtain the blood samples. You will be checked closely to see if complications due to blood drawing occur. Possible risks of blood draws may include bruising, swelling, fainting, bleeding, formation of small blood clot and/or infection at the needle insertion site.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You may not directly benefit from participating in this study. Studies such as these may lead to new treatment approaches in the future. The future benefits of this study include gaining knowledge about how melanoma tumors respond to treatment and the best methods for following this disease by imaging.

What other choices do I have if I do not participate?

Taking part in this study is voluntary. Refusal to take part will not result in any penalty to you. You may have an FDG PET/CT scan or other standard imaging scans as part of your clinical care without participating in this study. You may receive standard therapy for your melanoma without participating in this study. You may also participate in the Penn Melanoma Tissue Collection Program without participating in this imaging trial.

Talk to your doctor about your choices before you decide if you will take part in this study.

Will I be paid for being in this study?

The cost of parking is covered for the days of the research FDG PET/CT scans and the day of the research biopsy, if you have one. In addition, you will receive $100 after completion of the second scan (FDG 2), which will be done after approximately 1 week of treatment with pembrolizumab.

Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

The baseline FDG PET/CT is considered a "research" scan, done only for the purpose of this study and it will be paid for by the study budget. You or your insurance company will not be billed for this scan. In some cases it will be ordered as a standard part of your medical care for melanoma and will be paid for by you and/or your insurance as they would be if you were not participating in this study. You and/or your insurance company will pay all medical expenses related to the treatment and standard clinical procedures ordered by your doctor as part of your melanoma care.

The 2nd FDG PET/CT that will be done about 1 week after you start treatment is considered a "research" scan, done only for the purpose of this study and it will be paid for by the study budget. You or your insurance company will not be billed for this scan.

The 3rd FDG PET/CT scan that will be done more than 10 weeks after you start treatment will be ordered clinically by your doctor as part of your standard clinical care. In some cases MRI or CT imaging may be used instead of FDG PET/CT. You and/or your insurance company will pay for this scan.

If you have one additional research blood draw as part of this study the cost of the blood draw, processing and any research tests completed using the blood will be paid for by the study.

If you have one additional research tumor biopsy done after you start treatment as part of this study the cost of the tumor biopsy, processing and any research tests completed using the tumor tissue will be paid for by the study.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We 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 the University of Pennsylvania or Merck & Co, Inc to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

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

When is the Study over? Can I leave the Study before it ends?

Your active participation in the study will end after you have completed the 3rd imaging study (FDG PET/CT, MRI, or CT scan), which is the scan performed after more than 10 weeks of treatment with pembrolizumab. We will continue to follow your medical records to gather information about your melanoma treatment for as long as you are receiving care for your cancer.

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.

If you decide not to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

This section of the consent will cover:

- What personal health information about you will be collected in this study
- Who will use your information within the institution and why
- Who may disclose your information and to whom

- Your rights to access research information about you
- Your right to withdraw your authorization (approval) for any future use of your personal health information

1. Personal health information about you that will be collected in this study

The following personal health information will be collected, used for research and may be disclosed or released during your involvement with this research study:

- Name
- Address
- Telephone number
- Electronic mail addresses
- Date of Birth
- Medical Record Number
- Health plan ID numbers
- Any other unique identifying number, characteristic, or code
- Current and past medications or therapies
- Information from the tests and procedures described earlier in this document
- Results from laboratory tests, pathology results and radiology tests related to your cancer diagnosis or treatment

2. Why is my personal health information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right

3. Who may use and share information about me?

The following individuals and organizations may use or disclose your personal health information for this research project:

- The Principal Investigator and the Investigator's study team (other University staff associated with the study)
- The University of Pennsylvania Office of Human Research (the office which monitors research studies)
- Authorized members of the University of Pennsylvania and the University of Pennsylvania Health System and School of Medicine workforce who may need to access your information in the performance of their duties, for example: to provide treatment, to ensure integrity of the research, accounting or billing matters, etc.
- A description of this 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 it will include a summary of the results. You can search this web site at any time.

4. Who, outside of the University of Pennsylvania Health System and the School of Medicine, might receive my personal health information?

As part of the study the Principal Investigator, study team and others listed above in item number 3, may disclose your personal health information, including the results of the research study tests and procedures to the following:

- The University of Pennsylvania Institutional Review Boards (the committees charged with overseeing research on human subjects) and University of Pennsylvania Office of Regulatory Affairs

In all disclosures outside of the University of Pennsylvania Health System and School of Medicine, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law.

5. How long will the University of Pennsylvania Health System and the School of Medicine be able to use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. This information may be maintained in a research repository (database). However, the University of Pennsylvania Health System and School of Medicine may not re-use or re-disclose your personal health information collected in this study for another purpose other than the research described in this document unless you have given written permission for the Principal Investigator to do so. However, the University of Pennsylvania Institutional Review Board may grant permission to the Principal Investigator or others to use your information for another purpose after ensuring that appropriate privacy safeguards are in place. The Institutional Review Board is a committee whose job it is to protect the safety and privacy of research subjects. Results of all tests and procedures done solely for this research study and not as part of your regular care will not be included in your medical record.

6. Access to your records

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

7. Changing your mind

You may withdraw from the study for any reason simply by explaining this to the Principal Investigator or a member of the study team. Withdrawal will not interfere with your future care.

You may also withdraw your permission for the use and disclosure of any of your personal information for research, **but you must do so in writing** to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your personal information that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission to use your personal health information that means you will also be withdrawn from the research study.

Who can I call about my rights as a research subject?

If you have questions regarding your participation in this research study or if you have any questions about your rights as a research subject don't hesitate to speak with the Principal Investigator listed on page one of this form. Concerning your rights as a research subject, you may also contact the Office of Regulatory Affairs at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date
_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date

Consent for use or collection of blood and pathology tissue for research purposes

What am I being asked to do?

As part of the imaging study we would like to collect pathology tissue from cancer biopsies to be able to compare results to our experimental imaging studies. We would also like to collect an additional blood sample for research purposes.

If you agree to allow collection of biopsy tissue for the purposes of this study there are different types of tissue collection that may occur. You may choose to agree to all of the choices below, select the choices you do agree to or choose not to agree to any of them. This choice will not affect your ability to participate in the imaging study, however, it may determine which imaging group you are eligible to be part of in the study. Even if you agree to these procedures the study doctor may decide not to perform the procedures if your disease is not easily accessible for biopsy or if there would not be enough tissue available for clinical diagnosis and treatment decisions.

Making your choice:

Please read each sentence below about allowing access to pathology tissue that has been collected from sites of your primary or metastatic cancer and think about your choice. After reading each sentence, check the box next to "Yes" or "No." No matter what you decide to do, it will not affect your care. If you have any questions, please talk to your doctor or nurse, or call the Principal Investigator listed on the first page of this consent form. If you have any questions about your rights as a research subject, call the University of Pennsylvania Institutional Review Board (IRB) at (215) 898-2614.

1. **I have consented to participate in a research program called "Penn Melanoma Tissue Collection Program (IRB #703001)" and I give permission for my study ID number to be shared with the study team for this protocol. I give permission for any tissue that has been collected as part of the Penn Melanoma Tissue Collection Program protocol to be accessed and used for the purposes of this research study if there is adequate tissue available to learn about, prevent, treat or cure melanoma, associated disease and treatment related conditions.**

   □ Yes □ No

   IF THE ANSWER TO QUESTION #1 IS NO PLEASE CHECK NO TO QUESTIONS 2-5

2. Research tissue collected during clinical biopsy procedure

If your doctor has ordered a biopsy or surgical staging procedure as part of your standard clinical care we are asking your permission to collect additional tissue at the time of the procedure that will be stored and used for the purposes of this research study. Even if you agree to this tissue collection if there is not enough tissue available at the time of the procedure for research then no tissue will be collected for this study. If you are not scheduled for a clinical biopsy you may be asked to undergo a research biopsy of a site of disease selected by an investigator.

I consent to allow collection of additional tissue for this research study at the time of my clinical biopsy or surgical procedure or to have a research only biopsy performed for the purposes of this study. I give permission for any tissue that is collected to be stored and used for the purposes of this research study.

□ **Yes** □ **No**

3. **I consent to allow my "archival" tissue from prior and/or future biopsy or surgery procedures may be used for this research study to learn about, prevent, treat or cure melanoma, associated disease and treatment related conditions.**

□ **Yes** □ **No**

4. **I consent to allow the study team may contact UPHS and/or the non-UPHS healthcare entity that currently houses tissue sample(s) from any biopsy or surgical procedure related to my cancer diagnosis or treatment. The study team may ask this entity about acquiring a tissue sample, which is in excess of what would be required for clinical care, for research use at the University of Pennsylvania. This tissue may be used for this research to learn about, prevent, treat or cure melanoma, associated disease and treatment related conditions.**

□ **Yes** □ **No**

5. **I consent to allow an additional blood sample to be taken and stored for the purposes of this research study.**

□ **Yes** □ **No**

PLEASE INITIAL THE STATEMENT BELOW IF YOU HAVE ANSWERED YES TO ANY OF THE QUESTIONS 1-5 ABOVE:

I am aware that the tissue needed for this protocol may deplete (entirely use up) the tissue, in which case it will not be available for my future clinical care

Patient Initials: _____

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date

_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date