Informed Consent Form

Winship3321-16: Phase Ib Trial of Pembrolizumab and XL888 in Patients with Advanced Gastrointestinal Malignancies

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EMORY UNIVERSITY | Institutional Review Board
Research Administration

EMORY | WINSHIP CANCER INSTITUTE
A Cancer Center Designated by the National Cancer Institute

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 and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Winship 3321-16: **Phase II** trial of Pembrolizumab and XL888 in Patients with Advanced Gastrointestinal Malignancies

Principal Investigator: Bassel El-Rayes, MD

Investigator-Sponsor: Bassel El-Rayes, MD

Study-Supporter: Merck & Co. Inc. and Exelixis; NIH - National Institute of Health

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?

The purpose of this study is to define the activity of combining two research drugs pembrolizumab (also known as MK-3475) and XL888 in two independent groups of patients. First group with advanced stage pancreatic cancer and second group with advanced stage colorectal cancer. XL888 is a new anti-cancer drug now being studied in several clinical trials. XL888 is not approved by the U.S. Food and Drug Administration (FDA) for any GI cancers. Pembrolizumab has been approved for use in certain types of melanoma, head and neck squamous cell carcinoma and non-small cell lung cancer; however, it has not been approved by the U.S. Food and Drug Administration (FDA) for advanced gastrointestinal cancer.

We plan to enroll up to 94 patients on this trial. The trial has two parts. In the first part, which was recently completed, we demonstrated that the combination of pembrolizumab at 200 mg intravenously every three weeks can be safely combined with XL888 at 90mg by mouth twice a week. We did not

observe any new or increased risks of known toxicities associated with each drug when used in combination.

You are being considered for the second part of the study. In the second part of the trial, we plan to enroll an additional 32 patients. These will include 16 patients with pancreatic cancer and 16 patents with colorectal cancers. During the first 21 days (cycle 1) patients will be randomly assigned to receive either pembrolizumab only or the combination of pembrolizumab and XL888. After cycle 1 is completed everybody on the study will receive the combination.

In addition, we plan to enroll 8 patients with pancreas cancer and 8 patients with colorectal cancer to a paired biopsy study. These patients will receive a biopsy prior to start of treatment and a repeat biopsy at prior to cycle 2 between days 15 and 21 after starting therapy. The biopsies are intended for us to understand how these drugs work. The results from the analysis of these biopsies will not change your medical care. Participation in the paired biopsy study is voluntary.

What will I be asked to do?

All subjects must sign an informed consent document prior to the initiation of any study related procedures. The informed consent document must be signed within 28 days of Cycle 1 Day 1.

Screening procedures (with the exception of the scans) are to be conducted within 28 days of starting the study (Cycle 1 Day 1).

- Medical History
- Record concomitant medications taken up to 28 days prior to day 1 cycle 1
- Vitals [temperature, heart rate (HR), blood pressure (BP) and respiratory rate (RR)]
- Physical Examination, including height and weight
- Collect samples for
  - Safety tests- thyroid function, blood counts, triglycerides, cholesterol, blood sugar, liver and kidney functions
  - Serum or urine pregnancy test for women of childbearing potential
  - Tumor markers(when applicable such as known elevated tumor markers): CEA, CA19-9, or α-fetoprotein
  - HIV, HBsAg, HCV RNA if clinically indicated and urinalysis
- 12-lead ECG
- Eye exam
- Radiologic imaging studies to evaluate tumor status. contrast computed tomography (CT) or magnetic resonance imaging (MRI) of the chest and abdomen and pelvis.
- Baseline fresh biopsy (in selected group) will be obtained with 28 days of day1 cycle 1 and after consent is signed.

Days 1 (+3 days) of each cycle (Cycle is 21 days)

- Record concomitant medications
- Vitals (temperature, heart rate, blood pressure and respiratory rate)
- History and physical exam
- Assessment for side effects
- 12 lead ECG cycle 1, cycle 2 and every other cycle after XL888 administration
- Laboratory Assessments
  - Blood tests – routine – blood counts, liver and kidney function

- Tumor markers - when applicable
- Thyroid blood test cycle 2 and then after every 3 cycle

- Blood sample 20 cc for correlative work (only cycle 1, 2, 3)

- Patients will receive either
  1. Pembrolizumab 200 mg will be administered as a 30 minute IV infusion every 3 weeks.
     OR

  2. Pembrolizumab 200 mg will be administered as a 30 minute IV infusion every 3 weeks and XL888 90 mg will be administered orally

Days 4, 8, 11, 15, and 18 of each cycle (Cycle is 21 days)
- XL888 dose administered and diary completed

Day 8 and 15 of 1st cycle only
- Record concomitant medications
- Vitals (temperature, heart rate, blood pressure and respiratory rate)
- History and physical exam
- Assessment for side effects
- Laboratory Assessments
  - Blood tests – routine – blood counts, liver and kidney function
  - Blood sample 20 cc for correlative work (Day 15 only)

Between days 14 and 21 of cycle 1
Repeat biopsy in selected cases

Day1 cycle 2 and beyond
Pembrolizumab 200 mg will be administered as a 30 minute IV infusion every 3 weeks
XL888 90 mg will be administered orally

Every 3 cycles between day 15 and 21
- Repeat cross sectional imaging (CT or MRI)

End of treatment visit
- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam
- ECOG performance status
- Toxicity assessment
- Laboratory Assessments
  - Blood tests – routine – blood counts, liver and kidney function and urine analysis
  - Tumor markers - when applicable
  - Thyroid blood test cycle 2 and then after every 3 cycle
- Blood sample 20 cc for correlative work

Subjects will stay on the trial until either cancer gets worse (disease progression), significant side effects (toxicity) or withdrawal of consent.

Safety Follow-Up Visit

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.

After you complete the 30-day follow-up 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 you will continue to come in for a follow-up visit every 6 weeks with clinic visit and imaging until your cancer gets worse or you start a new treatment for your cancer. After 1 year, the imaging time will occur every 9 weeks (± 7 days).

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

Subjects who are eligible for retreatment with pembrolizumab/ XL888 may have up to two safety follow-up visits, one after the Treatment Period and one after the Second Course Phase.

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 and administer 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.

What are the possible risks and discomforts?
There may be side effects from the study drug or procedures that are not known at this time.

Seville orange, star fruit, grapefruit and their juices can affect the activity and concomitant use with XL888 should be avoided.

Side effects of **XL888** include:

The most common risks and discomforts expected in this study are:
- Diarrhea
- Feeling tired
- Feeling sick to your stomach

- Weakness
- Throwing up
- Decreased appetite
- Abdominal pain

Rare but serious side effect:
- Visual disturbances- blurred vision and/ or decreased vision including visual loss and blindness
- Decreased liver functions measured by blood tests

Uncommon Side Effects
Although uncommon, patients have experienced serious side effects such as pneumonia (infection in the lung); radiation skin injury (inflammation of skin in an area that was previously radiated); bowel obstruction and pain.

Preliminary results from non-human based studies indicate that XL888 may cause the heart muscle to take longer than usual to make another beat. This is called QT prolongation. QT prolongation is determined by an electrocardiogram (ECG). This prolongation could predispose patients to develop symptoms such as fainting (syncope) or an arrhythmia (a disturbance in your heart rate) which can potentially be fatal. While taking part in this study, your doctor may request additional electrocardiograms (ECG, EKG) to monitor your heart rate and rhythm.

Side effects of **pembrolizumab/KEYTRUDA** include:

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.

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

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

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

- Joint Pain
- 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 level of salt in the blood that may cause you to feel tired, confused, headache, muscle cramps or sick to your stomach

UNCOMMON
(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
(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 an multisystem inflammatory disorder characterized by visual changes, and it is often associated with changes in skin color cutaneous manifestations, including headache, and hearing loss.
- Vasculitis is an inflammation of the blood vessels. It happens when the body's immune system attacks the blood vessels. Symptoms include fever, fatigue, and muscle and joint pain. Other parts of the body can be affected as well.
- Sclerosing cholangitis is an inflammation of the bile ducts in the liver. This will led to scarring of the bile ducts. Symptoms include yellow discoloration (jaundice) of skin and eyes, itching and abdominal pain. In severe cases can lead to liver failure.

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

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.

What effects could the tests have on me?

Electrocardiogram (ECG): May cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin.

CT Scan: The contrast solution that may be given for a CT scan may cause an allergic reaction (rare). Severe allergic reactions can be life threatening. CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated (lost body water) or elderly.

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.

Radiation-Related Risks: You will be exposed to radiation from CT scans. Some of these procedures are not necessary for your medical care and will occur because you participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 4 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

Tumor Biopsy: Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy, perforation of gastric wall/esophagus 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.

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 become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. 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 and for 120 days after the last dose of study medicine. 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 the study drug 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 taking the study drug and for 4 months after the last dose. You and the study doctor should agree on a method of birth control to use throughout the study.

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.

Will I benefit directly from the study?

Your cancer may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about the safety of the combination of pembrolizumab and XL888. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

You will get $45 for each completed study clinic visit, to compensate you for your time and effort. If you do not finish the study, we will compensate you for the study clinic visits you have completed. You will get $585 total, if you complete all 13 study visits. You may be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study. These options include other clinical trials or chemotherapy drugs including regorafenib and TAS-102 for colorectal cancer; and liposomal irinotecan for pancreatic cancer, some of which have demonstrated a survival advantage. The study doctor will discuss these with you. You do not have to be in this study to be treated for your cancer.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?

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.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), including your de-identified genetic information, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Your data [and specimens] from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data or specimens are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Medical Record

If you have been an Emory and Saint Joseph's Hospital patient before, then you already have an Emory and Saint Joseph's Hospital medical record. If you have never been an Emory and Saint Joseph's Hospital patient, you do not have one. An Emory and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital 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 and Saint Joseph's Hospital medical record you have now or any time during the study.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: results on the correlative blood samples and results on the analysis of the tumor biopsy specimens.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory and Saint Joseph's Hospital will help you to get medical treatment. Emory and Saint Joseph's Hospital 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 and Saint Joseph's Hospital 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. Bassel El-Rayes at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs

Pembrolizumab and XL888 will be free of charge. Paired biopsies will be free of charge.

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 and Saint Joseph's Hospital will submit claims to your insurance for items and services that the sponsor does not cover. Emory and Saint Joseph's Hospital 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 Saint Joseph's Hospital 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 and Saint Joseph's Hospital 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.

Conflict of Interest

This project is receiving study support from Merck and is evaluating Merck pharmaceuticals. Dr. Bassel El-Rayes serves as a consultant to Merck and receives compensation for these services. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict of interest policies.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

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 and Saint Joseph's Hospital may use and disclose your PHI to get payment for study related treatment and 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.
- Bassel El-Rayes 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 and Saint Joseph's Hospital 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: Office for Human Research Protections and Food and Drug Administration
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
    - Study –Supporter: Merck & Co. Inc. and Exelixis
- 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 for Paired Biopsy Studies

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:

- 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 for Optional Study:
We will use and disclose your PHI for the conduct and oversight of the optional research study.

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 following people and groups will use and disclose your PHI in connection with the optional research 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:

Bassel El-Rayes, MD
Winship Cancer Institute, Emory University
1365-C 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 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. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

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.

<u>Contact Information</u>
Contact Bassel El-Rayes 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

Consent and HIPAA Authorization for Optional Study:
Please initial below if you opt to participate in and authorize use and disclosure of your PHI in the optional study previously described:

Paired Biopsy Studies

_____Initials

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 Person Conducting Informed Consent Discussion **Date** **Time (please circle)**