Informed Consent Form

A Phase 2 Study of Docetaxel, Ramucirumab, and Pembrolizumab for Patients with Metastatic or Recurrent Non-Small Cell Lung Cancer who Progressed on Platinum-Doublet and PD-1/PD-L1 Blockade

NCT Number: NCT04340882

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You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 30 people who are being studied, at Emory and elsewhere.

Why is this study being done?

This study is being done to determine whether it is safe and effective to shrink your lung cancer by combining three drugs each one with different mechanisms of action: docetaxel works mainly by stopping cancer cells from dividing; ramucirumab blocks new blood vessel growth to reduce tumor growth; and pembrolizumab helps the body's immune system to attack cancer cells and hinder their ability to grow and spread. You are being asked to be in this research study because you have incurable non-small cell lung cancer that continued to grow after treatment with platinum-based chemotherapy and immune therapy.

Do you have to be in the study?

It is your choice to join this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you choose, take time to learn about the study.

What do you have to do if you choose to join this study?

If you qualify and chose to join the study, you will get the three study drugs (docetaxel, ramucirumab, and pembrolizumab) until your disease gets worse, or death, or the side effects of the study drugs become unacceptable, or your doctor believes the study is not in your best interest anymore, or you withdraw consent for any reason.

While in the study, the researchers will also ask you to do the following: physical examination, take measurement of your vital signs, blood samples drawn, urine test, appropriate imaging scans; tissue biopsy (optional). Some of these procedures and pembrolizumab will be paid for by the study; ramucirumab, docetaxel and standard of care procedures will be billed to your insurance.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question. Given this is an investigational treatment, there is no guarantee that you will derive benefit if you choose to participate in this study.

What are the risks or discomforts you should know about before deciding?

The study will take time. The drug combination that is being tested may not work any better than regular care and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious such as:

- fatigue, nausea, vomiting, diarrhea, constipation, decreased appetite, rash, cough, shortness of breath, fever, hair loss, inflammation of the nerves, mouth, or any other organ in the body, low blood count, infection, high blood pressure, seizures, bleeding
- loss of privacy
- breach of confidentiality

You can find a detailed list of expected risks, their frequency and severity in the section titled "What are the possible risks and discomforts?" of this document. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Alternatives to Joining This Study

If you decide not to enter this study, there is care available to you outside of this research study. Your doctor will discuss alternative options with you. You do not have to be in this study to be treated for your cancer.

Costs

You WILL have to pay for some of the study procedures, in particular those that are not covered by your medical insurance. The study team can help you work out how much you might have to pay. There is more information in the "Costs" section further below.

What Should You Do Next?

Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions such as how much time you will have to spend on the study, any words you do not understand and more details about study procedures. Make sure you understand which parts of the study are research and which are standard care that you would have even if you did not join the study. Take time to think about this and talk about it with your family and friends.

Emory University and Grady Health System
Consent to be a Research Subject / HIPAA Authorization

Title: A phase 2 study of docetaxel, ramucirumab, and pembrolizumab for patients with metastatic or recurrent non-small cell lung cancer who progressed on platinum-doublet and PD-1/PD-L1 blockade

IRB #: STUDY0000030

Principal Investigator: Badi El Osta, MD

Investigator-Sponsor: Badi El Osta, MD

Study-Supporter: Merck

Introduction
You are being asked to be in a medical research study. This form tells you what you need to think about before you choose if you want to join the study. **It is your choice. If you choose to join, you can change your mind later and leave the study.** Your choice will not cause you to lose any medical benefits. If you choose not to join this study, your doctor will still treat you.

Before you decide:
- Read this form or have it read to you
- Listen to the study doctor or study staff explain the study to you
- Ask questions about anything that is not clear

You will get a copy of this form. Take your time to think about joining the study. You may wish to discuss it with family or friends. Do not sign this form if you still have questions or something does not 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?
This study will help the study doctors find out if combining three drugs (docetaxel, ramucirumab, and pembrolizumab) is a better way to treat your lung cancer. The study doctors hope to learn whether the study drug combination will be safe and will shrink your cancer and enable you to live longer.

What will you be asked to do?
This study asks you to do several things, most of them would be done as standard of care if you were not on this study. After you sign this Informed Consent form and before starting treatment, you will be asked to:
• Review your health history and ask how you are feeling
• Conduct a physical exam including vital signs
• Have baseline testing of your organ function (by collecting blood and urine samples). If you are a woman of child-bearing potential, you will be asked to have a pregnancy test
• Have a PET/CT or computerized tomography (CT) scan or magnetic resonance imaging (MRI) or bone scan to see tumor
• Go over your past and current medications
• Ask you for tissue samples of your tumor and blood tests for research purposes.

Prior to each treatment you will have laboratory tests (blood and/or urine) and an evaluation including physical exam by your treating physician. If you are a woman of child-bearing potential, you will be asked to have a pregnancy test.

Once on treatment, you will receive three study drugs called docetaxel, ramucirumab, and pembrolizumab through your vein (IV) once every three weeks (every 21 days). On the first day of each cycle, docetaxel and ramucirumab will be given IV over 60 minutes each, and pembrolizumab will be given IV over 30 min.

We would also collect about 2 tablespoons (30 ml) of blood for research purposes:
- On Cycle 1 Day 1 prior to drug administration
- On Cycle 2 Day 1 prior to drug administration
- At the end of treatment (discontinuation visit)

Imaging scans will be performed within 28 days of starting your treatment, then during the treatment period, imaging scans will be performed approximately 6 weeks from the start date. Subsequent tumor imaging will be performed every 6-12 weeks or more frequently if clinically indicated. Imaging will continue to be performed until disease progression is identified by your physician.

In the circumstance you will discontinue the study treatment, tumor imaging should be performed at the time of treatment discontinuation.

During your time on study, you can be seen by your care provider in clinic. Once you are off study, you will receive a phone call to determine current status every 3 months for 2 years then every 6 months for the next 3 years then annually until disease recurrence, initiation of new cancer therapy or lost to follow-up whichever occurs first.

How will your study drug be provided?
The study drug 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 study drug to you. If you have questions about the study drug, you should ask the principal investigator or study nurse. You may also call the pharmacy at [redacted] if you have questions about the study drug. The number for the pharmacy is included on your study drug package, if given one.

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

Additional tumor and blood samples will be obtained and used for medical research by the investigators of this study. These samples are valuable to medical research and may help identify a marker to help with the treatment of this disease. The samples are coded to protect your identity. Samples will not be sold or used directly for the production of commercial products.

What are the possible risks and discomforts?
To our knowledge, the combination of docetaxel, ramucirumab, and pembrolizumab has not been previously tested. There may be side effects from this three-drug combination or procedures that are not known at this time.

General Risks

If you choose to take part in this study, there is a risk that the study approach may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:
- Spend more time in the hospital or doctor's office
- Be asked sensitive or private questions about things you normally do not discuss.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 6 months after you have completed the study.
The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

- 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, and some may never go away
- Some side effects may make it hard for you to have children
- Some side effects may be mild, serious, and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect
- Your study doctor will work with you to treat your side effects
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

The following adverse events are associated with the use of

<u>Ramucirumab:</u>

- Cardiovascular: high blood pressure, blood clot, heart attack
- Blood: low white blood cell count, anemia, low platelet count, bleeding
- Respiratory: nose bleeding
- Gastrointestinal: diarrhea, inflamed mouth, mouth sores
- Kidneys: protein loss in urine
- Endocrine & metabolic: low sodium, low calcium, decreased appetite, decreased albumin
- Central nervous system: headache
- Immunologic: Antibody development
- Dermatologic: rash, non-malignant tumor on the skin involving blood vessels similar to a birthmark, hair loss, redness, pain or peeling of palms and soles
- Miscellaneous: Infusion related reaction, fatigue, watering eyes
- Thyroid Dysfunction: decreased thyroid function

Rare but serious adverse events have occurred such as:

- Heart failure which may cause shortness of breath, chest pain, swelling of ankles, and tiredness
- Stroke which may cause paralysis, weakness, or headache
- Blockage of the bowels which may cause pain, or vomiting
- A tear or hole in the stomach and/or bowel which may cause pain and may require surgery
- Damage to the liver which may cause damage to the kidneys, pain, bleeding, swelling of arms and/or legs and/or abdomen, or confusion
- Severe blood infection
- Reversible damage to the brain which may cause headache, changes in thinking, decreased vision, and/or seizures
- Difficulty speaking or change in voice

Ramucirumab combined with docetaxel is an FDA-approved therapy for patients with non-small cell lung cancer. In this combination the most common serious adverse reactions were low neutrophils count, fever, pneumonia.

The most common adverse reactions observed in treated patients were low neutrophils count, fatigue, high blood pressure, nose bleeding, inflammation of the mouth, and diarrhea.
Clinically relevant adverse drug reactions reported in ≥1% and <5% of ramucirumab with docetaxel-treated patients were low sodium in blood, and protein loss in urine.

Docetaxel:
The most serious adverse reactions from docetaxel are liver toxicity, low neutrophils count, allergic reaction, and fluid retention. The most common adverse reactions are infections, low neutrophils count, anemia, low platelets count, fever, allergic reaction, neuropathy, problems with taste, shortness of breath, constipation, loss of appetite, nail disorders, fluid retention, fatigue, pain, nausea, diarrhea, vomiting, inflammation of mouth, hair loss, skin reactions, and muscle aches. Allergic reactions and development of another cancer are rare.

Pembrolizumab:
Pembrolizumab is generally well tolerated and demonstrated a favorable safety profile in comparison to chemotherapy. The important identified risks for pembrolizumab monotherapy are primarily of an immune-mediated nature. They can occur even after discontinuation of treatment and can affect any and more than one body system simultaneously. Severe and fatal cases are rare. In clinical studies, these adverse events were reversible and managed with interruptions of pembrolizumab, administration of corticosteroids, and/or supportive care.

Immune mediated adverse reactions include inflammation of any organs such as the lungs (pneumonitis), colon (colitis), liver (hepatitis), kidneys (nephritis), hormone glands (such as thyroid, adrenal, pituitary glands) and Type I diabetes mellitus). Other rare immune-mediated adverse reactions were reported in <1% of patients treated with pembrolizumab were:
- Inflammation of the eyes (uveitis)
- Inflammation or swelling of the nerve fibers of the eye which send visual information from the eye to the brain (optic neuritis)
- Inflammation of the muscles (myositis)
- Inflammation of the joints (arthritis)
- Inflammation of the pancreas (pancreatitis)
- Inflammation of the heart muscle (myocarditis)
- Inflammation of the sac around the heart (pericarditis)
- Inflammation of the nerves (Guillain-Barré syndrome, myasthenic syndrome, myasthenia gravis (including exacerbation)

• Inflammation of the brain (encephalitis)
• Inflammation of the spinal cord (myelitis)
• Inflammation of the blood vessels (vasculitis). Symptoms will depend on the particular blood vessels that are involved in the inflammatory process; for example, if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue
• Hypoparathyroidism or low levels of parathyroid hormone (a hormone made by four tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling or burning in your fingertips, toes, or lips
• Inflammation of the stomach (gastritis). You may have pain in your belly, feel full, or sick to your stomach. You may also experience nausea, vomiting or loss of appetite.

• Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, or have a fast heartbeat. You may also experience difficulty with physical exercise, pale or yellow skin, dark urine, or fever.

• Not enough pancreatic enzymes (proteins that break down food) that leads to poor digestion of food (exocrine pancreatic insufficiency). You may have bloating, gas, discomfort in your belly, diarrhea, abnormal stool that is oily, or weight loss.
• Inflammation and scarring of the bile ducts (sclerosing cholangitis)
• Growth of inflammatory cells most commonly in lungs, lymph nodes, eyes and skin (sarcoidosis) or making too many activated immune cells (hemophagocytic lymphohistiocytosis or HLH)
• Other severe skin reactions, some with fatal outcomes; and
• Transplant rejection.

Myelitis or inflammation of the spinal cord is a new identified risk in the specific population of renal cancer patients who received the combination of pembrolizumab with axitinib, another drug that blocks new blood vessel growth.

Most common adverse reactions (reported in ≥20% of patients) were fatigue, musculoskeletal pain, decreased appetite, itching, diarrhea, nausea, rash, fever, cough, shortness of breath, constipation, pain, and abdominal pain.

Pembrolizumab in combination with chemotherapy: fatigue, nausea, vomiting, constipation, diarrhea, decreased appetite, rash, cough, shortness of breath, fever, loss of hair, neuropathy, inflammation of mouth.

Pembrolizumab in combination with ramucirumab: diarrhea, fatigue, high blood pressure, decreased thyroid function.

Researchers may learn something new during the study that may affect your choice to be in the study. If this happens, they will tell you about it. Then you can choose if you want to stay in this study. You may be asked to sign a new form if you choose to stay in the study.

What effects could the tests have on me?
You may feel discomfort during some of these tests or may experience some inconvenience. 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 (inside the vein): may cause discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely infection, nausea, and lightheadedness.

Magnetic resonance imaging (MRI) uses a strong magnetic field. You will be placed in a narrow cylinder, and this could make you feel claustrophobic. The magnetic field can move or alter any solid metal that you have in your body (e.g. pacemaker, artificial valves, joint replacements, cochlear implants or other medical devices). You should mention any such procedures you have had in the past to your doctors to determine whether there might be a risk from an MRI. If you have worked with metal in the past, you also should discuss the specifics with your doctor. An x-ray may be necessary to see whether there is metal left in your body.

Imaging with CT, PET/CT, and bone scans are used to create images of internal bones and organs using radiation. High dose radiation is known to produce cancer cells. The effect of exposure to radiation adds up over a lifetime. The amount of radiation exposure involved in this trial will not be significantly greater than for subjects with your disease who do not take part in the trial. The contrast solution that may be given for a CT scan may cause an allergic reaction (rare) and diarrhea. 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.

Radiation-Related Risks: You will be exposed to radiation from CT, PET/CT, or bone scans. These procedures are necessary for your medical care and will occur even if you do not 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 5 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.

Risks of biopsies: Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, bruising, swelling and scarring. Rarely, an infection or a perforation of an organ can occur.

If you are a woman: to protect against possible side effects of the study drugs, 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 until 6 months after last dose. If you think that you got 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 drugs 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 120 days 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 you benefit from the study?

This study is not designed to benefit you directly. While you are on study, your cancer may improve or stabilize, or may even get worse. This study is designed to learn more about how effective and safe this treatment is for patients with non-small cell lung cancer. The study results may be used to help others in the future.

Will you be paid for your time and effort?

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

What are your other options?

If you choose not to join this study, you can get care outside of this study. The study doctor will discuss these with you. You do not have to be in this study to be treated for your lung cancer.

If you choose to join this study, you may not be able to join other research studies. Discuss this with the researchers if you have concerns. You may wish to look on websites such as clinicaltrials.gov and ResearchMatch.org for other research studies you may want to join.

How will your private information be protected?

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.

Storing and Sharing your Information

We will store all the data and specimens that you provide using a code. We need this code so that we can keep track of your data over time. This code will not include information that can identify you (identifiers). Specifically, it will not include your name, initials, date of birth, or medical record number. We will keep a file that links this code to your identifiers in a secure location separate from the data. Despite these measures, we cannot guarantee anonymity of your personal data.

We will not allow your name and any other fact that might point to you to appear when we present or publish the results of this study.

Your data and specimens may be useful for other research being done by investigators at Emory and Grady Health System or elsewhere. We may share the data or specimens, linked by the study code, with other researchers at Emory and Grady Health System, or with researchers at other institutions that maintain at least the same level of data security that we maintain at Emory and Grady Health System. We will not share the link between the study code and your identity.

We will use your sample and data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

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

Emory and Grady Health System may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Grady Health System medical

records. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

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:

- Research blood collection
- Research tumor biopsy

Tests and procedures done at non-Emory and Grady Health System places may not become part of your Emory and Grady Health System 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 believe you have become ill or injured from this research, you should contact Dr. El Osta at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory and Grady Health System will help you to get medical treatment. Neither Emory and Grady Health System nor the sponsor have set aside money to pay for this medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

For Emory and Grady Health System, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory and Grady Health System employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

The sponsor will pay for certain items or services associated with the study.

The study sponsor will pay for certain items and services that you may receive if you take part in this study.

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 Grady Health System will submit claims to your insurance for items and services that the sponsor does not cover. Emory and Grady Health System 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 Grady Health System 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 Grady Health System 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
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 last planned study visit, the researchers may ask you to complete some of the final steps such as lab work or imaging as applicable.

The researchers also have the right to take you out of the study without your consent for any reason. They may do this if they believe it is in your best interest or if you do not agree to changes that may be made in the study.

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. If you do not sign this form, 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 Grady Health System 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.
- The study team 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 Grady Health System 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 and Grady Health System IRB, the Emory and Grady Health System Research and Healthcare Compliance Offices, and the Emory and Grady Health System Office for Clinical Research.
    - The study supporter: Merck.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
- 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 Studies: Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in the optional studies, the study doctor for the main study would like to collect **blood samples** and **samples of your tumor** for research.

If you choose to take part, a sample of tissue from your previously or newly collected biopsy and blood samples will be collected. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”.

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 for the optional studies. If you do not authorize the use and disclosure of your PHI for the optional studies, then you may not participate in the optional research study, but you can still be in the main research study.

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: [redacted].

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.

How is my Genetic Information Protected? What are the Risks?
The Genetic Information Nondiscrimination Act (GINA) is a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that GINA does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege
In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

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

If you have questions about the study procedures, appointments, research-related injuries or bad reactions, or other questions or concerns about the research or your part in it, contact:

Contact Dr. Badi El Osta 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.

This study has been reviewed by an ethics committee to ensure the protection of research participants. If you have questions about your **rights as a research participant**, or if you have **complaints** about the research or an issue you would rather discuss with someone outside the research team, contact the Emory Institutional Review Board at [redacted]

To tell the IRB about your experience as a research participant, fill out the Research Participant Survey at https://tinyurl.com/ycewgkke.

If you are a patient receiving care from the Grady Health System and have a question about your rights, you may contact the Office of Research Administration at [redacted]

Consent and Authorization

Consent and HIPAA Authorization for Optional Study/Studies: Please circle your choice of "YES" or "NO" and initial if you opt to participate in and authorize use and disclosure of your PHI in the optional studies previously described:

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory studies described.

Optional research blood collection:

YES ..... (Initials) NO ..... (Initials)

Optional paired research blood collection and tumor biopsy (Emory participants only):

YES ..... (Initials) NO ..... (Initials)

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES ..... (Initials) NO ..... (Initials)

TO BE FILLED OUT BY SUBJECT ONLY

Print your name, **sign**, and **date** below if you choose to be in this research study. You will not give up any of your legal rights by signing this form. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____

Signature of Subject (18 or older and able to consent) **Date** **Time**

_____ _____

Signature of Legally Authorized Representative **Date** **Time**

_____

Authority of Legally Authorized Representative or Relationship to Subject

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____

Signature of Person Conducting Informed Consent Discussion **Date** **Time**