Informed Consent Form

A Phase 2 Study of Neoadjuvant Cabozantinib in Patients with Locally Advanced Non-metastatic Clear Cell Renal Cell Carcinoma

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EMORY | WINSHIP CANCER INSTITUTE

A Cancer Center Designated by the National Cancer Institute

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 20 people who are being studied, at Emory.

Why is this study being done?
This study is being done to answer the question: will taking cabozantinib be effective in treating kidney cancer before surgery? You are being asked to be in this research study because you have kidney cancer.

Do you have to be in the study?
It is your decision to be part of 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 make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?
If you are eligible and want to be part of the study, you will participate for up to 3 years. The researchers will ask you to do the following: physical examination, including height and weight; taking measurement of your vital signs, an electrocardiogram (EKG or ECG), blood samples drawn, Echocardiogram or MUGA, scans (CT or MRI) performed. Some of these procedures will be paid for by the study.

How is this study going to help you?
If you are in the study, you will be helping the researchers answer the study question. The study results may be used to help others in the future.

What are the risks or discomforts I should know about before making a decision?
The study will take time. The drug 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 – for this study, these include: inflammation of the liver cells, high elevation of blood pressure, Nephrotic syndrome-damage to the kidney leading to the too much loss of protein in the urine, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the “What are the possible risks and discomforts?” section of this document.

Alternatives to Joining This Study
If you decide not to enter this study, there is care available to you outside of this research study. The study doctor will discuss these 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 cost section below.

What Should I 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 (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand which parts of these are research and which are standard care that you would have even if you did not join the study. 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: Winship4643-19: A Phase 2 Study of Neoadjuvant Cabozantinib in Patients with Locally Advanced Non-metastatic Clear Cell Renal Cell Carcinoma

Principal Investigator: Mehmet Asim Bilen, MD

Co-Principal Investigator: Viraj Master, MD, PhD

Study-Supporter: Exelixis

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 determine the effectiveness of cabozantinib in kidney cancer before surgery. Cabozantinib is approved for treatment of advanced stage kidney cancer by the U.S. Food and Drug administration (FDA).

Tumor biopsies are required for participation, which is frequently performed for renal tumors, and will be performed before initiation of treatment for each patient from the kidney cancer, and will be used for diagnosis and research. Additional tissue will be collected at the time of surgery when the cancer is removed, and is already out of the body. Biopsies are important to understand whether cabozantinib is affecting the tumor microenvironment.

We plan to enroll approximately 20 patients on this trial.

Patients will be started on cabozantinib 60mg by mouth daily for total of 12 weeks. The doses of cabozantinib you start could be lowered or held if you experience serious side effects.

What will I be asked to do?

All subjects must sign an informed consent document prior to initiation of any study related procedures. The informed consent document must be signed within 28 days of first dose of study treatment.

Screening procedures are to be conducted within 28 days of starting the study.

- Informed Consent
- 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
- Performance assessment
- Collect samples for
    - Safety tests- thyroid function, blood counts, blood sugar, coagulation, pancreas, liver and kidney functions
    - Urine pregnancy test for women of childbearing potential within 72 hours of study drug
    - Thyroid function test
    - Inflammation test (C-reactive protein)
    - Urinalysis and urine protein to creatinine ratio
- 12-lead ECG
- Echocardiogram or MUGA if clinically indicated
- Radiologic imaging studies to evaluate tumor status. Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain, chest and abdomen/pelvis (Those imaging studies will also be used for muscle and fat assessment).
- Baseline biopsy from kidney mass after the consent is signed and before the trial treatment is started for research. If not available, biopsy will also be used to confirmed diagnosis of kidney cancer and presence of clear cell component.

Treatment procedures

Day 1 of week 1 (within 14 days before the first dose of study treatment)

- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam, including weight
- Performance assessment
- Collect samples for
    - Blood counts, blood sugar, coagulation, pancreas, liver and kidney functions
    - Urine pregnancy test for women of childbearing potential within 72 hours of study drug
    - Inflammation test (C-reactive protein)
    - Urinalysis and urine protein to creatinine ratio
- Research blood sample (up to 60cc)
- Cabozantinib will start to be taken by mouth

- 12-lead ECG
- Quality of life questionnaires and frailty assessment

Day 1 of week 2 (± 5 days)

- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam, including weight, pill diary and pill count
- Performance assessment
- Collect samples for
    - Blood counts, blood sugar, pancreas, liver and kidney functions
    - Inflammation test (C-reactive protein)
- Cabozantinib taken by mouth

Day 1 week 6 (± 5 days)

- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam, including weight, pill diary and pill count
- Performance assessment
- Collect samples for
    - Blood counts, blood sugar, coagulation, pancreas, liver and kidney functions
    - Urine pregnancy test for women of childbearing potential within 72 hours of study drug
    - Inflammation test (C-reactive protein)
    - Urinalysis and urine protein to creatinine ratio
    - Thyroid function test
- Research blood sample (up to 60cc)
- Cabozantinib taken by mouth
- 12-lead ECG
- Radiologic imaging studies to evaluate tumor status. Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain, chest and abdomen/pelvis (Those imaging studies will also be used for muscle and fat assessment).
- Quality of life questionnaires and frailty assessment

Post- Treatment Period (End of 12 weeks [within 14 days after last study treatment dose])

- Record concomitant medications
- Vitals (temperature, HR, BP and RR)
- History and physical exam, including weight, pill diary and pill count
- Performance assessment
- Collect samples for
    - Blood counts, blood sugar, coagulation, pancreas, liver and kidney functions
    - Serum or urine pregnancy test for women of childbearing potential within 72 hours of study drug
    - Inflammation test (C-reactive protein)
    - Urinalysis and urine protein to creatinine ratio
    - Thyroid function test
- Research blood sample (up to 60cc)
- 12-lead ECG

- Radiologic imaging studies to evaluate tumor status. Computed tomography (CT) or magnetic resonance imaging (MRI) of the brain, chest and abdomen/pelvis (Those imaging studies can be done within 28 days after last study treatment dose and will also be used for muscle and fat assessment).
- Quality of life questionnaires and frailty assessment
- Preparation for kidney surgery will be done per standard of care
- Patients will undergo kidney surgery no earlier than 28 days after the last dose of cabozantinib and research tissue will be obtained from surgical sample

Long-Term

- After kidney surgery, patients will enter long term follow-up period and can be seen by medical oncology or urology team via clinic visit, chart review, or phone call to determine current status every 3 months (+/- 14 days) until disease recurrence, initiation of new antineoplastic or investigational therapy whichever occurs first.
- Research blood sample (approximately 60cc) will be collected after surgery
- Surveillance scan after surgery will be obtained per investigator based on routine clinical guidelines.

You will take cabozantinib for 12 weeks or until significant side effects (toxicity) or withdrawal of consent. Cabozantinib must be taken on an empty stomach. You must be instructed not to eat for at least 2 hours before and at least 1 hour after taking cabozantinib. You should be instructed to take cabozantinib dose at approximately the same time every day. If you miss a dose, the dose may be taken later only if it is within 12 hours of when the missed dose should have been taken. The missed dose should not be made up if it is within 12 hours of the next scheduled dose.

How will my medicine be provided?

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

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may still be used for this study. Blood samples collection is mandatory, therefore there is no option to destroy samples.

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 oranges, star fruit, grapefruit and their juices can affect the activity and concomitant use with the study drugs should be avoided.

Side effects of cabozantinib include:
Cabozantinib, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, including advance kidney cancer. But it may not be approved to treat your type of cancer prior to surgery. When participating in clinical studies with an investigational drug, cancer patients may experience side effects related to the drug. In studies of cabozantinib given alone, side effects related to cabozantinib have been reported in patients with many different types of cancer.

The following is a comprehensive list of side effects reported as related to cabozantinib:

Very Common Side Effects that Occurred in ≥ 10% of Cancer Patients (≥ 1 in 10) Treated with Cabozantinib:

- Abdominal pain
- Alteration of thyroid function tests
- Blisters, rash, or pain in hands or feet
- Changes in blood tests used to monitor the liver, which may indicate liver damage
- Change in voice
- Changes to the way things taste
- Constipation
- Diarrhea
- Fatigue
- Hair color changes or hair loss
- High blood pressure
- Inflammation of mucus membranes
- Loss of appetite
- Mouth and throat sores or swelling
- Nausea
- Rash
- Vomiting
- Weakness
- Weight loss

Common Side Effects That Occurred ≥ 1% but < 10% of Cancer Patients (≥ 1 in 100, but < 1 in 10) Treated with Cabozantinib:

- Abnormal thickening of the outer layer of the skin
- Change in the feeling of touch
- Cough
- Bleeding, including bleeding from stomach or intestines which may look like coffee grounds or black sticky bowel movements and bleeding within the brain
- Blood clot in a large vein, usually in the leg
- Blood clot that travels from a vein to the lung
- Confusion and disorientation
- Decreased amounts of red blood cells (anemia), which may cause feelings of tiredness or shortness of breath
- Decreased amounts of calcium or sodium in the blood
- Decreased or increased amounts of potassium in the blood
- Decreased amounts of magnesium or phosphorus in the blood
- Decreased level of albumin in the blood

- Decreased platelet counts, which increases the risk of bleeding or make bleeding more difficult to stop
- Decreased white blood cell counts, which may increase chances of infection
- Dermatitis acneiform, a type of acne
- Dehydration
- Difficulty swallowing
- Dizziness
- Dry mouth
- Dry skin
- Fever
- Fungal infections including mouth, lung, and other locations
- Hemorrhoids and bleeding hemorrhoids
- Headache
- Increased amounts of pancreas enzymes in the blood, which may indicate damage to the pancreas
- Increased levels of bilirubin in the blood, which may indicate complications with the liver
- Increased levels of creatinine in the blood, which may indicate complications with the kidneys
- Mouth or throat pain
- Muscle spasm
- Muscle weakness
- Pain in a joint or muscle
- Pain in extremities
- Protein in the urine, which may indicate kidney damage
- Shortness of breath
- Stomach acid coming up from the stomach into the esophagus
- Swelling of the limb(s)
- Ulcer
- Upset stomach or indigestion

Uncommon Side Effects That Occurred ≥ 0.1% but < 1% of Cancer Patients (≥ 1 in 1000, but < 1 in 100) Treated with Cabozantinib:

- Abnormal electrical activity in the heart that could cause a potentially serious change in heart rhythm
- Abnormal opening between two organs or from an organ to the outside of the body
- Abscesses (infected cavities filled with pus)
- Blood clot in an artery
- Chest discomfort originating from the heart
- Clouding of the lens in the eye that affects vision
- Damage to skeletal muscle tissue
- Decreased brain function or decreased alertness and ability to think
- Decrease in all blood counts (red blood cells, white blood cells and platelets)
- Destruction of bone tissue, in particular, bone in the jaw
- Feelings of unease or fear
- Gallstones
- Heart attack
- Heart failure
- Holes in the stomach or intestines
- Infections

- Inflammation of the intestine, appendix, gall bladder or thin tissue lining the inner wall of the abdomen and most of the abdominal organs
- Reduced kidney function
- Liver failure
- Loss of consciousness, fainting episode
- Pneumonia and inflammation of the lungs
- Rapid heart rhythm
- Re-opening of wounds after surgery
- Respiratory failure
- Seizure
- Stroke / mini-stroke
- Tear or inflammation in skin that lines the anus
- Uncoordinated movements

Rare but Medically important Side Effects not listed above that Occurred ≥ 0.01% but < 0.1% of Cancer Patients (≥ 1 in 10000, but < 1 in 1000) Treated with Cabozantinib:

- Air in the chest between lungs and chest wall
- Allergic reaction
- Anemia caused by destruction of red blood cells
- Blocked intestines
- Blood vessel inflammation associated with possible bleeding, bruising, and/or rash
- Brain dysfunction caused by brain swelling
- Cancer of the mouth or skin
- Damage to the outermost surface of the eye
- Enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall
- Inflammation and blockage of channels that carry bile from the liver
- Severe swelling of the mouth, lips, tongue, eyes and throat, or difficulty swallowing or breathing
- Temporary paralysis of the intestines
- Throat swelling
- Very high blood pressure that comes on suddenly and quickly and which can lead to serious injury to the heart and brain

What effects could the tests have on me?

Risk of blood drawing and intravenous access: Putting a tube or needle in your vein to draw blood or give you drugs may hurt when the needle is put in. There is a risk of continued pain, bruising, dizziness, fainting or infection, which although rare, can occur.

Electrocardiogram (ECG): Small pads are attached to your skin in order to record the electrical activity of your heart. The ECG itself is painless, however it may cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin. Sometimes it may be necessary to shave small areas of the chest in male patients in order to attach the ECG leads.

Contrast Agents: Your CT or MRI procedure will require the use of a “contrast agent.” The contrast agent is a substance that helps the radiologist interpret the images. The contrast agent will be injected by either a hand-held needle or a machine that does the injection. Most contrast agents stay in your body for only a few minutes, but some of them can remain for a few hours or days without any harm

to you or anyone near you. Contrast agents are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The contrast agent could affect kidney function or cause an allergic reaction, though these outcomes are rare. The contrast agent could also leak from your veins a little causing swelling and discomfort, that is typically treated with ice packs.

Magnetic Resonance Imaging (MRI): MRI exams use powerful magnets to create images of the body. In addition to the possible reactions to contrast materials, you may feel claustrophobic while in the magnet, and will hear loud beeping or hammering noises. If you have tattoos or any metal items in your body such as implants, pacemakers, clips or shrapnel, we will do special screening to make sure your MRI scan is done safely.

MUGA

For your MUGA scan, a small amount of radioactive material will be injected by either a hand-held needle or a machine. Such injections are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The radioactive material could also leak from your veins a little, causing swelling and discomfort. After injection and a waiting period for the drug to circulate within your body, you will be asked to lie very still for several minutes while the scan takes place.

Radiation-Related Risks: You will be exposed to radiation from nuclear medicine and CT 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 2 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, and very 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. The tumor biopsy will be performed by radiologists at Emory University.

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 an adequate birth control method or abstinence 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 an adequate method of birth control or abstinence to use throughout the study.

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

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

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 effects of cabozantinib prior to kidney surgery. The study results may be used to help others in the future.

Will I be compensated for my time and effort?
You will not be offered compensation for being in this study.

What are my other options?
If you decide not to enter this study, there is care available to you outside of this research study. 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.

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
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.

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.

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.

Emory and Saint Joseph's Hospital 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 Saint Joseph's Hospital medical record. 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: results on the correlative blood samples and results on the analysis of 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 believe you have become ill or injured from this research, you should contact Dr. Bilen 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 Saint Joseph's will help you to get medical treatment. Neither Emory, Saint Joseph's nor the sponsor will pay for your 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.

Emory, Saint Joseph's and the sponsor have not, however, set aside any money to pay you if you are injured as a result of being in this study or to pay for this medical treatment. For Emory and Saint Joseph's, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or Saint Joseph's 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 study sponsor will pay for certain items and services that you may receive if you take part in this study.

Cabozantinib 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.

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.

Human Biological Samples

While you are in this study, you will have blood (serum/plasma) and biopsy samples collected to be used for the current study analysis, including re-running study tests, if necessary, and storing samples for future research. Blood samples collection is mandatory, therefore there is no option to destroy samples. The purpose of storing these samples is to make them available to scientists who are trying to develop new tests, treatments, and ways to prevent diseases. We hope that these samples and images will provide information that will help researchers in the future. The samples will be labeled with an identification code. Your samples and images will never be labeled with your name and will remain separate from the files linked to your name.
Successful research using the samples or other parts of the samples could result in a commercial or therapeutic product with significant value, such as a product for the medical treatment or diagnosis of cancer or other disorders. You will not share in any financial benefits of these uses.

Your samples will only be used for research and will not be sold. These samples may be utilized by Emory and Saint Joseph's Hospital for further or additional analyses to answer scientific or medical questions, but if your samples or images are given to other researchers (other than Emory and Saint Joseph's Hospital) your samples would only be given to researchers who have had their research reviewed by an Institutional Review Board (IRB), which is a committee that protects the rights and privacy of study subjects.

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 study in which you may choose to participate.

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 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.
- 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 Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.

  - Research monitors and reviewer.
  - Accreditation agencies.
  - Study-Supporter: 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.

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:

Mehmet Asim Bilen, 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.

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 Dr. Bilen 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] or [redacted] or [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

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study, and any optional studies you initialed above. 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)**