Informed Consent Form

Winship4221-17: Phase II Study of IMRT Re-Irradiation with Concurrent/Adjuvant Nivolumab in Patients with Locoregionally Recurrent or Second Primary Squamous Cell Cancer of the Head and Neck

NCT Number: NCT03521570

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You Are Being Asked to Be in a Research Study

What Is a Research Study?

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

Do I Have to Do This?

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

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

What Is This Document?

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

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

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

What Should I Do Next?

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

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: Phase II study of IMRT re-irradiation with concurrent/adjuvant nivolumab in patients with locoregionally recurrent or second primary squamous cell cancer of the head and neck

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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 test the effect of an immunotherapy drug called nivolumab when added to radiation therapy on controlling your cancer. Nivolumab has been approved by the FDA in the treatment of advanced head and neck cancer that cannot be controlled with radiation or surgery and that has failed the standard chemotherapy used to treat head and neck cancer.

This study is testing nivolumab in a different situation. Your doctors are recommending repeat radiation for your cancer. Often this is given as the only treatment. In this trial we will be combining nivolumab with radiation therapy to treat your cancer and we will give you nivolumab for a total of one year after finishing radiation therapy. This study will test whether nivolumab can help treat your cancer more effectively and reduce the chance of your cancer coming back compared to our prior cure rates with radiation alone. While nivolumab is FDA approved for the treatment of head and neck cancer, it has not been used in patients who need repeated radiation to treat head and neck cancer (like yourself). We therefore do not know what effect, if any, nivolumab will have on reducing the chance of your disease coming back.

What will I be asked to do?

There are three periods to the study: screening, treatment, and follow-up periods.

Screening Period

This period may include more than one study visit for various procedures. At the Screening Visit you will be asked to read and sign this informed consent before any study related procedures that are not standard of care are performed. It is your right as a subject to have the study fully explained to you and you can ask that your study doctor explain or go over any parts of this informed consent that you do not understand.

The following tests and procedures will be performed by the study staff to determine if you qualify to participate in this study. Unless otherwise stated, these exams, tests, or procedures are part of regular cancer care and may be done even if you do not join the study.

1- Review of your medical history.
2- Review of medications you are currently taking and have taken in the past including herbal medications.
3- A physical examination including measurement of your height, weight and vital signs (temperature, blood pressure, and heart rate).
4- You will be asked about the symptoms you are having from your disease, this procedure is also called determination of your performance status.
5- Collection of your blood for laboratory tests which measure your blood chemistry, including kidney and liver function, count your red and white blood cells and platelets, and check for PT/PTT/INR. Your tumor may be tested for human papillomavirus (HPV) if not known depending on the location of your original tumor.
6- A blood test for research purposes will also be obtained before treatment starts.
7- If you have had a tumor biopsy/cancer surgery in the past, your study doctor will request the original samples from the medical facility where it was done. In order to participate in this study, you must provide your permission to obtain these original samples and allow your study doctor to send them to a laboratory for research testing. If no biopsy was performed after your cancer came back you will asked to have a biopsy performed of your tumor or one of its metastatic lymph nodes; if needed, this biopsy would be performed for research purposes only.
8- A computed tomography (CT) scan or PET scan or MRI of head and neck, brain, chest, and all other known areas of disease will be done. These are special procedures which use X-rays (in the case of CT) or magnetic fields (in the case of MRI) to create pictures of the inside of your body. These pictures will allow your doctor to monitor your disease before, during, and after you receive radiation and nivolumab.
9- A urine or blood pregnancy test for women of childbearing potential must be performed before the first dose of study medication is given. Results of the pregnancy test must be negative for you to participate in this study.

10- You will be asked to answer questions that assess your quality of life during the study. This questionnaire is for research purposes only.

About 51 subjects are expected to participate in this study from different participating institutions. Emory plans to enroll close to 25 subjects. Even though you may meet all the criteria for participation, it is possible that you will not be enrolled in this study.

If, based on the results of the screening visit tests and procedures, you qualify to participate in the study, you will return to the study doctor's office for the Baseline Visit.

Treatment Period
If you qualify to participate in the study based on the results of the screening visit tests and procedures, you will return to the study doctor's office/clinic. You will then begin therapy.

Nivolumab will be given as an intravenous (IV) infusion that takes approximately half an hour (30 minutes). Intravenous infusion means that the drug is administered as a liquid substance directly into a vein. A pump will be used for the intravenous infusions to ensure the correct amount of medicine is given over the proper amount of time. Nivolumab will be given every 2 weeks starting 2 weeks before radiation therapy and continue to be given every 2 weeks during radiation therapy (which takes 6.5 weeks). After your radiation treatment is completed, nivolumab will be given once every 4 weeks until the treatment is completed (1 year after beginning radiation). The nivolumab dose you will receive after radiation treatment will be a higher dose to account for the fact that nivolumab will be given every 4 weeks instead of 2 weeks.

Radiation therapy: will be given daily excluding weekends for a total of six to six and a half weeks.

One cycle of therapy consists of 4 weeks; before and during radiation this will consist of 2 infusions of nivolumab. After radiation, one cycle will be equivalent to one infusion of nivolumab every 4 weeks.

If you experience any changes in your body or develop any new or worsening side effects during or after the infusion you should inform the study doctor or nurse immediately.

During the Treatment Period, at the beginning and end of radiation therapy as well as weeks 18, 30, 52 and 104 of the study, you will be asked questions about your condition including:

1- How your cancer is affecting your daily activities.
2- What medications you have taken or are currently taking including herbal supplements and over-the-counter medicines.
3- What side effects you have experienced. During your clinic visits, you should report the development of any new or worsening medical problems (since your last visit) to the study doctor or other study personnel taking care of you.

The following procedures/samples will be performed and/or collected at 1 or more visits:

1- A brief physical examination, including body weight and examination of performance status every 2 weeks during radiation therapy (on the days you receive nivolumab) and every 4 weeks after radiation is completed until finishing the treatment.
2- Vital sign measurements (blood pressure, heart rate, weight) will be assessed on the day of infusion. If you develop a reaction during the infusion, you will continue to have your vital signs measured until the study doctor determines it is no longer necessary.

3- Blood samples will be drawn to assess 1 or more of the following:
   - Blood chemistry, including kidney and liver function, red and white blood cells and platelets count, and coagulation tests (PT/PTT/INR), in order to measure the effect of nivolumab on your immune system. These tests will take place every 2 weeks during radiation therapy (on the days you receive nivolumab) and every 4 weeks after radiation is completed until finishing the treatment.
   - Collection of blood (approximately 8ml every 2 weeks during radiation therapy and at Weeks 18, 3052, 104 which equals approximately 3 tablespoons) for biomarker tests (substances in your blood such as cells, proteins, DNA, RNA, or other markers). Measuring biomarkers in the blood could help predict whether or not someone is likely to benefit from the drug in combination with radiation in future. These biomarker studies are for research purposes only.
4- A CT scan or PET /CT or an MRI of your neck as well as any other areas of disease or potential disease spread will be obtained at weeks 18, 30,52 and 104 of your treatment, or at any time if your disease has worsened or you stop receiving the study treatment (whichever occurs later).
5- Another biopsy of your cancer (if it is persistent) will be obtained at the end of treatment if clinically feasible. This may be at the end of the one year of treatment with nivolumab or in case your cancer returns (relapses) before the end of treatment on the study. The biopsy is for research purposes and will help us understand better the way nivolumab works with radiation therapy and its effect on your immune system's ability to fight cancer. The biopsy results will not affect the way you are treated but may influence treatment of future patients.

You may be discontinued from receiving study treatment based on your disease assessments or if you are having side effects that make you unable to tolerate study therapy. Based on discussions between you and your study doctor, you may discontinue for other reasons including your decision to stop being treated.

Follow-up Period
After completing all study treatments or after you are withdrawn from treatment, you will be asked to continue with follow-up visits to monitor for side effects or potential benefits you may be experiencing from study treatment as per our usual cancer care. Your total participation in this study from the time you have signed the informed consent to your last study visit, including follow-up visits, will be about two years (depending on how your cancer responds to the treatment and how well you tolerate the treatment). However, your doctors will continue to see you in follow up after the completion of the study as per their normal cancer care routine.

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 will be kept and will still be used for this study. However is you request to destroy these samples we will do so.

What are the possible risks and discomforts?
Treatments for cancer often have side effects, including some that are life-threatening. There is the possibility of death occurring as a result of this treatment and its side effects. There may be additional unknown risks from participating in this study and receiving Nivolumab. If you experience severe side effects associated with the study drug, your doctor

may prescribe medications to treat the side effect(s), future treatments may be delayed, or treatment may be stopped permanently. Any significant new findings that develop during the course of the research and may relate to your willingness to continue participation will be provided to you:

Nivolumab side effects:
Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse right away about any possible side effects you experience.

The most common risks and discomforts expected are (> or = to 15%):

- Fatigue
- Rash
- Abdominal pain
- Increased levels of markers associated with liver function abnormalities (alkaline phosphatase, ALT, AST)
- Increased levels of markers associated with pancreas inflammation (amylase, lipase)
- Increased levels of markers associated with decreased kidney function (creatinine)
- Chills
- Constipation
- Cough
- Decreased appetite
- Diarrhea
- Dry mouth
- Dry skin
- Fever
- Headache
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Itching
- Joint pain or stiffness
- Loss of color (pigment) from areas of skin
- Lung inflammation (pneumonitis - see details below)
- Musculoskeletal pain
- Nausea
- Shortness of breath
- Swelling, including face, arms, and legs
- Thyroid gland function decreased or increased
- Thyroid stimulating hormone increased: lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Vomiting

The less common risks and discomforts expected are (between 5-15%):

- Adrenal gland function decreased
- Allergic reaction
- Bilirubin (liver function blood test) increased
- Bronchitis
- Cranial nerve disorder

- Diabetes
- Dizziness
- Dry eye
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Increased blood sugar
- Inflammation of the eye
- Inflammation of the heart or its lining
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Liver inflammation
- Low blood pressure
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Redness
- Renal failure
- Respiratory failure
- Sodium levels in blood low
- Upper respiratory tract infection
- Vertigo
- Vision blurred

Rare but possible risks include (<5%):

- Anaphylactic reaction (severe allergic reaction)
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids and diabetic coma
- Erythema multiforme: skin inflammatory reaction
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of blood vessels
- Inflammation of the brain, potentially life-threatening or fatal
- Lung infiltrates, associated with infection or inflammation
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin

- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.
- Lung inflammation (pneumonitis): This adverse effect has been reported infrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue. Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest x- rays and/or CT scans.
- Complications, including fatal events, have occurred in patients who received allogeneic hematopoietic stem cell transplant (HSCT) before or after nivolumab. Complications, including rejection, have also been reported in patients who have received an organ or tissue transplant.
- Treatment with nivolumab may increase the risk of the organ or tissue transplant. Please inform your study doctor or nurse AT ONCE if you experience any of the following:
    - Any new or increased shortness of breath;
    - Any new or increased chest pain;
    - Any new or increased pain/difficulty while breathing;
    - Any new or increased cough or any significant change in your type of cough; for example any new or increased mucous or blood in your cough;
    - Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.
- If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.
  Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab treatment, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

Radiation Risks
Risks and side effects related to the **radiation** include those which are:

Likely (20% or greater of the time)
- Dry mouth
- Loss of taste buds
- Thick saliva
- A skin burn that looks like a sunburn
- Fatigue
- Pain requiring numbing or pain medicine

Less Likely (occurs 10-20% of the time)
- Unable to eat requiring a feeding tube

- IV fluids for dehydration
- Scar tissue in neck
- Difficulty opening your mouth
- Swallowing difficulty with big bites and dry food

Rare but serious (2-10% of the time)

- Bleeding or Carotid blowout – leaky blood vessel in your neck that can bleed. A carotid blowout can be fatal.
- Infection
- Non healing wound
- Mandible necrosis – the jaw bone gets weak or fractures
- Teeth damage/loss
- Permanent feeding tube
- Permanent breathing tube
- Death
- Radiation induced cancer

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

Other Risks

Side effects associated with blood draws or use of an IV catheter may include infection, fainting, bruising, redness, discomfort, or bleeding at the needle puncture site.

Risks and side effects associated with a biopsy depend on the type of biopsy done. A core needle biopsy may cause pain at the insertion site, some swelling, or some bruising around the insertion site. A surgical biopsy may cause pain or bruising at the incision site, a possible reaction to anesthesia or numbing agents, irritation from stitches or staples, and the possibility of infection.

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.

Contrast Agents

Your CT or MRI procedure may require the use of a contrast agent, which 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, which is typically treated with ice packs.

PET

If you receive a PET 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.

There may be additional risks or side effects which are unknown at this time. Your condition may not get better or may become worse while you are in this study. Certain drugs may increase the severity of these side effects if taken during the study. Ask your study doctor for a full list of prohibited medications.

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. 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 31 weeks 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?

This study is not designed to benefit you directly. Nivolumab is an approved therapy for your cancer and is recommended by treatment guidelines and is a widely used standard therapy for head and neck cancer. However, it has not been used in combination with repeat radiation before. It may or may not help the radiation work better at helping kill your cancer and preventing it from coming back. You may or may not derive any benefit from participating in the study. Your participation in the study will teach us about this treatment and what we learn may help other patients with head and neck cancer 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. Other treatments available for your condition include

1- Getting treatment or care for your cancer without being in a study. This can include getting radiation on its own or getting radiation with another medication combination.
2- Taking part in another study of an investigational drug
3- Getting supportive treatment only without any cancer directed therapy.

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

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

Your samples, genomic data and health information will be stored and shared with other researchers. The samples and information will be available for any research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from.

Medical Record

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

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

Emory Healthcare 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 Healthcare 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 of biomarker studies on blood and biopsy samples

Tests and procedures done at non-Emory places may not become part of your Emory 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 will help you get medical treatment. Emory and the study supporter have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or study supporter 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. Saba at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs

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

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

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

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

Withdrawal from the Study

Your participation in this study is entirely voluntary. It is up to you to decide whether to take part or not. Even if you do decide to take part, you are free to partially or completely end your participation in the study. An example of partially ending your participation would be to discontinue only your receiving of study treatments. You may completely or partially end your participation at any time without giving a reason. This will not affect your future medical care in any way. You may decide not to participate or to participate and later quit the study without penalty or loss of benefits to which you are otherwise entitled.

Please note that any information collected before you withdraw will be kept and used to complete the research.

If you decide to stop study treatments, your study doctor will not presume that you have withdrawn from the study, but will assume that you will continue to participate in any follow-up activities. If you do not want to participate in any or all follow-up activities, you should inform your study doctor. For your safety, however, you should consider the study doctor's advice about how to go off the study treatment.

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 this research study includes:

- Information such as your name, address, contact details, date of birth, race, ethnic origin, and your life habits.
- 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. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

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

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

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

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to 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 research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory, Cleveland Clinic, and University of Wisconsin 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, the Emory Office for Clinical Research, the Emory Clinical Trials Audit & Compliance Office, the Emory Radiation Safety Committee, and similar offices at the Cleveland Clinic and University of Wisconsin.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.

- Accreditation agencies.
- Study-supporter: Bristol-Myers Squibb

- 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: Consent to Additional Tumor Biopsy for research purposes:

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 study. 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, 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:

Nabil Saba, MD
Department of Hematology and Medical Oncology
Emory University
1365-C Clifton Rd NE
Atlanta, Georgia 30322
United States

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 Information

Contact Dr. Saba (at Emory) at telephone number [redacted] or Dr Koyfman (at the Cleveland Clinic) 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 to Additional Tumor Biopsy for research purposes (Optional)

Signing below indicates that you have been informed about the possibility of an additional tumor biopsy to be done for this research study either before you start treatment on this study or in the event that your tumor fails to disappear or comes back during or after treatment. You do not have to consent to this additional biopsy to participate in this study.

Would you like to participate in this optional part of this study whereby you allow researchers to take an additional sample of your tumor either before treatment or if the tumors fails to disappear or grows back for additional research study?

Please mark one:

_____ Yes - I agree to allow an additional tumor biopsy to be done for research purposes if asked by my study doctors

_____ No - I do not agree to allow an additional tumor biopsy to be done for research purposes if asked by my study doctors

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)**