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School of Medicine

WAKE FOREST School of Medicine

Informed Consent Template

Department of Internal Medicine Section on Hematology and Oncology

Department of Radiation Oncology

Quad-Shot Radiotherapy in Combination with Immune Checkpoint Inhibition for Advanced/Recurrent Head and Neck Cancer

Principal Investigators: Mercedes Porosnicu MD, Ryan Hughes MD

SUMMARY

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have recurrent, metastatic, or advanced head and neck cancer, you are scheduled to be treated with pembrolizumab immunotherapy and you have at least one tumor that can be targeted with radiation treatment.

Your participation in this research will involve immunotherapy treatments which occur every 3 weeks. In addition, you will be treated with low-dose palliative radiation therapy during the immunotherapy. These include 4 total treatments given twice a day over 2 consecutive days in between immunotherapy treatments. You may receive at least 1 and up to 3 courses of this radiation therapy during this study. **Both of these treatments are considered standard for your cancer, but the combination of the two is the subject of this study.**

Participation in this study will involve treatment with immunotherapy in combination with low-dose radiotherapy commonly used for relieving symptoms from your cancer, called palliative radiotherapy. Both immunotherapy and palliative radiotherapy are standard for this type of cancer. All research studies involve some risks. A risk to this study that you should be aware of is that development of side-effects to immunotherapy or palliative radiotherapy may be more likely when combining them together as is done in this study. There is the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include participation in other clinical protocols, treatment with immunotherapy alone, treatment with palliative radiotherapy alone, or treatment with other drug therapies as per your physicians. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

This consent form gives you important information about this study to help you decide if you want to participate. It describes the purpose of this study, the study procedures, the possible risks, and provides information about your rights as a study participant. Please read this

description carefully. You should talk to the study doctor and her study staff about this study and ask to explain any words or information contained in this informed consent document that you do not understand and ask any questions you have. You can also discuss this study with other people such as your family or personal doctor. Please take your time in making your decision as to whether or not you wish to participate. If you decide to participate in this study, you will be asked to sign and date this form. You will receive a copy of the signed form.

The person in charge of this study is Dr. Mercedes Porosnicu, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is:

[redacted]

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US Law.

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have recurrent, metastatic, or advanced head and neck cancer and you are able to get immunotherapy and palliative radiotherapy according to your doctors. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

You have been asked to take part in this study because you have recurrent, metastatic, or advanced head and neck cancer. A standard treatment for your condition is drug treatment like immunotherapy. Another standard treatment for your condition is low-dose palliative radiotherapy to improve symptoms from your cancer. As you have already been informed, there is a chance that immunotherapy will not work for your cancer, and that palliative radiotherapy alone will not work for the cancer. Instead, it is to provide relief from symptoms being caused by the cancer. This may mean that the cancer grows and causes symptoms and complications in the future.

The purpose of this research study is to determine whether combining routine low-dose palliative radiation therapy with routine immunotherapy treatments can increase the chances of both

treatments working. Pembrolizumab is FDA-approved for the treatment of head and neck cancers like yours. This medication may activate your immune system that in many cases is silenced by cancer, to attack your cancer and stop it from growing. When the immune system is more active, it has a better chance to fight the cancer in your body. Palliative radiotherapy (as in this study) is also FDA-approved for your cancer. Radiation therapy can trigger faster cancer destruction in the area of radiation treatment and this can activate the immune system to further attack the cancer and stop it from growing. We expect that the combination of this palliative radiation therapy with immunotherapy will help the immunotherapy and radiotherapy to work better.

This study has two goals. One goal is to measure how effective the combination of immunotherapy and palliative radiotherapy is to stop the growth of your cancer. Another goal is to help find biologic molecules in the blood or saliva that may prove to be good indicators of how efficient this medication is against your cancer. Using samples of blood and saliva collected at several time points during the treatment, we plan to make special analyses in the lab in order to find changes that may explain how radiation therapy can help increase the effect of immunotherapy against the cancer.

How Many People Will Take Part in the Study?

21 people will take part in this study conducted at our Cancer Center.

What Is Involved in the Study?

If you take part in this study, you will

- Receive pembrolizumab every 3 weeks as you would during routine practice. The duration of this treatment is up to you and your medical oncologist, but generally lasts until it stops working or causes side effects that cause you to stop. An immunotherapy cycle is the dose of immunotherapy given every 3 weeks.
- Have the following tests and procedures prior to your first cycle of immunotherapy:
    - Demographic information and medical history, as part of routine care.
    - Physical exam, performance status assessment, routine laboratory blood tests, electrocardiogram, current medications, as part of routine care.
    - Imaging by CT scan and/or MRI of the tumor(s); a PET scan if approved by your medical insurance, as part of routine care.
    - Blood sample collection about two tablespoons of blood for research
    - Saliva sample collection for research
    - Pregnancy test for women of childbearing potential, as part of routine care.
    - As part of this study and routine care, you will be tested for HIV (human immunodeficiency virus, which is the virus that causes the acquired immunodeficiency syndrome [AIDS]); Hepatitis A, B, and C. You will be told of the results of the testing, and counseled as to the meaning of the results, whether they are positive or negative. If the test indicates that you are infected with one of these diseases, you will receive additional counseling about the significance of your care and possible risks to other people. We are required by law to report all

positive results of HIV test to the North Carolina State Board of Health. The test results will be released only as permitted by applicable law. If you do not want to be tested for these diseases, you should not agree to participate in this study.

- Have the following tests and procedures during each immunotherapy treatment visit:
  - Receive pembrolizumab through a vein (peripheral or central line) administered over approximately 30 minutes, as part of routine care.
  - Blood sample collection before each of the first five cycles of immunotherapy, as part of the study.
  - Saliva sample collection before each of the first five cycles of immunotherapy, as part of the study.
  - Complete a quality-of-life assessment, as part of the study.
- Have the following procedures between cycles 2-3 or 3-4 of immunotherapy:
  - Radiation treatments: 4 total treatments delivered twice a day, at least 6 hours apart, for 2 consecutive business days, as part of routine care. These treatments will not be delivered on the same day as immunotherapy infusions. We will aim to deliver the treatments within 7 days of your next upcoming immunotherapy cycle, as part of the study.
  - This will require a CT simulation scan (as part of routine care) in order to plan the radiotherapy done approximately 1-2 weeks prior to the delivery of radiation treatments.
  - Blood and saliva sample collection before the first administration of radiation treatment, as part of the study.
- Have the following tests between cycle 5-6 of immunotherapy:
  - Tumor assessment scans (CT and/or MRI imaging, or PET if approved by your insurance company), as part of routine care
- If the follow up scans show that there is still persistent tumor in the area of radiation treatment, another radiation treatment will be planned between cycle 6-7 of immunotherapy, if your radiation oncologist feels it is safe to deliver another course of radiation therapy:
  - Radiation treatments: 4 total treatments delivered twice a day, at least 6 hours apart, for 2 consecutive business days, as part of routine care. These treatments will not be delivered on the same day as immunotherapy infusions. We will aim to deliver the treatments within 7 days of your next upcoming immunotherapy cycle, as part of the study.
  - This may require a CT simulation scan in order to plan the radiotherapy done approximately 1-2 weeks prior to the delivery of radiation treatments, as part of routine care.
  - Blood and saliva samples will also be collected before the administration of immunotherapy number 6 and number 7 and before the first radiation treatment in the cases when the radiotherapy needs to be repeated, as part of the study.
- Have the following tests between cycle 10-11 of immunotherapy:
  - Tumor assessment scans (CT and/or MRI imaging, or PET if approved by your insurance company) , as part of routine care.
- If the follow up scans show that there is still persistent tumor in the area of radiation treatment, another radiation treatment will be planned between cycle 11-12 of

immunotherapy, if your radiation oncologist feels it is safe to deliver another course of radiation therapy:

- Radiation treatments: 4 total treatments delivered twice a day, at least 6 hours apart, for 2 consecutive business days, as part of routine care. These treatments will not be delivered on the same day as immunotherapy infusions. We will aim to deliver the treatments within 10 days of your next upcoming immunotherapy cycle, as part of the study.
- This may require a CT simulation scan in order to plan the radiotherapy done approximately 1-2 weeks prior to the delivery of radiation treatments, as part of routine care.
- Blood and saliva samples will also be collected before the administration of immunotherapy number 11 and number 12 and before the first radiation treatment in the cases when the radiotherapy needs to be repeated, as part of the study.

Blood and saliva sample collection will be done in a similar fashion at each visit, as part of the study.
5 ml of saliva will be collected by drooling into a large diameter tube, as part of this study.
You will have approximately 2 tablespoons – 35 ml of blood withdrawn from a vein at each specified time point as part of this study. The total amount of blood withdrawn during the study for research purpose will be approximately 12 tablespoons – 200 ml (7 ounces). In case that additional palliative radiotherapy is recommended, we will collect 6 additional tablespoons of blood for each radiation therapy course.

We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests and exams to your personal physician?

[ ] Yes [ ] No _____ Initials

Immunotherapy treatments will then proceed as they would according to routine practice. You and your doctor will decide on the duration of immunotherapy, depending on how well it works to keep your tumor under control.

Collection, Storage and Use of Biological Tissue

Testing the blood and saliva samples in the laboratory is one of the main purposes of this study.

Samples of blood and saliva will be collected as described in the previous section.

Participant blood samples will be used to isolate peripheral blood mononuclear cells (a fraction of the white blood cells) and the remaining serum or plasma, that may be analyzed for proteins and RNA using multiple methods. RNA is short for ribonucleic acid. RNA is a genetic material that has a major role in making proteins. Proteins are the building blocks of your body, cells, and organs. The isolated cells will be analyzed by single-cell RNA sequencing to identify the types of blood immune cells present and their states of activation over the course of treatment in this trial. This analysis provides a highly detailed evaluation of the status of the peripheral blood immune system in response to drug treatment. Study will also evaluate proteins in your blood and saliva modified in response to immunotherapy to measure the degree of response to treatment in your body. Bacterial RNA might be analyzed in your saliva to identify types of bacteria living in your mouth and how they change with treatment. Red blood cells isolated from your blood are left over and normally discarded might be utilized to practice and improve laboratory tests that are used to analyze changes in metabolism in cancer in general, including your type of cancer.

Your blood and saliva will be used only for research and will not be sold. The research done with your tissue and blood may help to develop new products in the future.

These samples will be kept and may be used in future research to learn more about other diseases. An Institutional Review Board (IRB) must also approve any future research study using your tissue samples. In order to participate in this study, you must be willing to provide these samples for future research.

Your *blood/saliva* samples will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES you may contact me for future research studies
____NO I do not want to be contacted regarding future research studies.

HOW LONG WILL I BE IN THE STUDY?

You will be in the treatment portion of the study for the duration of treatment with pembrolizumab and for additional 60 days after the last dose of pembrolizumab to monitor any treatment side-effects. However, we will continue to follow up your cancer condition and extract

information from your medical records and /or obtain information from you by phone.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

WHAT ARE THE RISKS OF THE STUDY?

The risks of this study are mainly related to the risks of **two standard of care treatments** for your type of head and neck cancer. These include risks of pembrolizumab and the risks of palliative radiotherapy.

The risks for each type of treatment are outlined in the section below. **This study is aimed to test how well the combination of pembrolizumab immunotherapy and palliative radiotherapy work together.** So, the risks of the study are basically the possibility of a higher chance of a side effect from *either* treatment occurring because they are being delivered in combination rather than just one treatment (or the other).

Consider the risks of either pembrolizumab or this type of radiation below. It is not clear that the combination of these two increases the chances of *any* of these side effects, but it is possible.

What is known about the safety of pembrolizumab in humans?

Adverse reactions in more than 10% of patients:

- Swelling of the arms or legs (11% to 15%), abnormal heart rhythm (11%)
- Itching of the skin (11% to 28%), skin rash (13% to 24%), change in skin coloration (vitiligo) (13%)
- High or low blood sugar (13% to 59%), changes in the blood electrolytes or proteins (10% to 46%), high cholesterol levels (33% to 43%), low thyroid function, weight loss (10% to 15%)
- Diarrhea (12% to 28%), decreased appetite (15% to 25%), constipation (12% to 22%), abdominal pain (13% to 22%), nausea (11% to 22%), vomiting (11% to 19%)
- Blood in the urine (12% to 19%), urinary tract infection (12% to 19%)
- Changes in the blood counts 1-54%
- Changes in the liver function tests (9% to 42%)
- Infection (16%)
- Fatigue (23% to 43%), pain (22%), headache (11% to 14%)
- Musculoskeletal pain (19% to 32%), joint pain (10% to 18%), muscle pains (12%), back pain (11% to 12%)
- Decreased kidney function (11% to 35%)
- Upper respiratory tract infection (13% to 28%), cough (14% to 26%), shortness-of-breath (10% to 23%), pneumonia (12%), flu-like symptoms (11%)
- Fever (10% to 28%)

Adverse events that are more rare than 10%:

- Selling of the face, inflammation or increased liquid in the lining surrounding the heart (pericarditis)
- Increased thyroid function (hyperthyroidism) or inflammation (thyroiditis)
- Difficulties swallowing (dysphagia), inflammation in the mouth (mucositis) or intestines (colitis)
- Inflammation in the liver (hepatitis), abnormalities in liver function tests, increased fluid in the abdomen (ascites)
- Tingling or pain or loss of function in the legs, arms or face (Peripheral neuropathy), insomnia, dizziness
- Neck pain, arthritis
- Acute renal failure
- Inflammation in the nose of throat (nasopharyngitis) or in the lungs (pneumonitis)
- Allergic reaction to the infusion of pembrolizumab

Adverse reactions resulting in permanent discontinuation occur in less than 5% of patients.

Severe and Fatal Immune-Mediated Adverse Reactions

Adverse reactions that are mediated by activation of your immune system by the study drug can sometimes be severe, can occur in any organ or part of your body, and can become life-threatening and lead to death, especially if left untreated. If you suffer any of these side effects described above (or any others not listed) or you think you are experiencing a side effect, during this study, please tell your Study Doctor immediately (see 'Who should you contact for more information?').

You will be followed closely by your Study Doctor for the entire time you are a part of this study. If you experience one of the side effects listed above or other new side effects, you will be treated right away with the medicines that have the best chance of helping the side effects.

If your cancer worsens, you will be treated in the manner you and your Study Doctor feel is best.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information.

There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

For blood draws, you may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

What are the risks of palliative radiotherapy in head and neck cancer patients?

The type of radiotherapy, palliative radiotherapy, that will be given in this study is used as part of routine care in the symptom control of patients with recurrent, advanced, or metastatic head and neck cancer. The treatment itself includes one to three "courses" of radiation treatment. Each course is made up of 4 individual radiation treatments, given twice a day, at least 6 hours apart, over 2 consecutive business days. All patients on this study will receive at least one "course" of palliative radiotherapy. Those who are able to safely receive more radiation AND do not have a good tumor response after the first round of scans may be eligible for a 2nd or 3rd course of radiotherapy.

Side effects of radiotherapy is related to the part of the body (or, head and neck) that is being treated. Please speak with your doctor about the potential risks and side effects of your personalized radiotherapy treatment.

In patients treated with 1-3 courses of this type of radiotherapy, about 5-35% of patients develop side effects, 0-14% develop severe side effects and less than 1-2% develop life-threatening side effects. The immediate (during and shortly after) side effects of radiation to the head and neck may include:

- Sore throat or mouth
- Skin irritation
- Dry mouth
- Taste changes
- Swallowing problems

The late (weeks to months after the radiotherapy) effects of radiation to the head and neck may include:

- Loss of hair in the treated area
- Cataracts
- Fluid behind the ear drums; decreased hearing
- Damage to the spinal cord, brainstem or brain
- Damage to nerves or blood vessels near the area treated
- Damage to bone and/or cartilage
  Damage to other normal tissues
- Induction of secondary cancers

WHAT DO I HAVE TO DO?

You must be willing to:

- Provide accurate and complete information about your medical history and your present condition.
- Follow the study procedures and keep all scheduled appointments. Inform the study team in advance if you have a problem with keeping an appointment.

- Tell the study team about any other medications (including herbal medications, vaccinations, and over-the-counter medications) you are taking and medical treatments you receive before and during the study. You may not take certain medications or receive certain medical treatments without the permission of the study team during the study or for up to 6 months.
- Tell your Study Doctor about any new side effect, injury, or symptom you experience.
- Tell your Study Doctor of any changes in current medical conditions. This information must be reported to your Study Doctor between study visits by using the contact numbers at the end of this consent form.
- You should not receive a live vaccination (one that uses live bacteria or viruses) within 30 days before or 30 days after receiving the study drugs.
- If you are female and from the time of informed consent through 1 year following the last dose of study medication you must agree to the following:

Reproductive Risks and other Issues to Participating in Research

Pembrolizumab can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death.

Additionally, radiation therapy can cause fetal harm. Radiation therapy is not generally given to pregnant females (except in extreme circumstances) due to these risks.

Avoid pregnancy unless you are unable to become pregnant (eg have had your “tubes tied”, had a hysterectomy or are at least 1-year post-menopausal). Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must agree to use two highly effective methods of birth control as noted in the table below (while taking the study drug and 1 year after that). Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions. Not engaging in sexual activity is an acceptable practice; however, occasional abstinence, the rhythm method and the withdrawal method are not acceptable methods of contraception.

Pregnant women are excluded from participation in this study. Because NO method of birth control is 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

Refrain from breastfeeding and egg cell donation for at least 1 year after the treatment.

Contraceptive Measures for Males

Your participation in this research study may damage your sperm, which could cause harm to a

child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study and for 3 months afterwards. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should also promptly notify her doctor.

Refrain from fathering a child or sperm donation.

If during the study and through 1 year following the last dose of study medication you learn that you are pregnant (female subject) or your female partner becomes pregnant (male subject), you must contact the Study Doctor immediately for further instructions about follow-up. The study team will ask you about any pregnancy during the study visits and may continue to follow-up with you for up to 60 days after your last dose of study medication. If at any time you report a pregnancy of either you or your partner, the study team will collect information about the results of the pregnancy and/or birth and will schedule any follow-up visits that may be necessary. This health information will become part of the clinical trial records and will be shared with the Sponsor so that the Sponsor may determine if there are any effects of the study medication on unborn children.

Highly Effective Methods of Birth Control

Barrier Methods	**Intrauterine device methods**	**Hormonal Methods**
Male condom plus spermicide Cap plus spermicide Diaphragm plus spermicide	Copper T Progesterone T (This is also considered a hormonal method) Levonorgestrel-releasing intrauterine system (eg, Mirena®) (This also is considered a hormonal method)	Implants Hormone shot or injection Combined pill Minipill Patch

As part of this study and part of routine care for patients treated with immunotherapy, you will be tested for HIV (human immunodeficiency virus, which is the virus that causes the acquired immunodeficiency syndrome [AIDS]), as well as for Hepatitis A, B, or C. You will be told of the results of the testing, and counseled as to the meaning of the results, whether they are positive or negative. If the test indicates that you are infected with one of the viruses mentioned above, you will receive additional counseling about the significance of your care and possible risks to other people. We are required by law to report all HIV positive results to the North Carolina State Board of Health. The test results will be released only as permitted by applicable law. If you do not want to be tested for HIV, you should not agree to participate in this study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope that treatment with pembrolizumab plus radiation therapy might help limit the progression of your cancer and improve the amount it responds to treatment. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. You may be eligible for one treatment, or the other, but not both combined like it is in this study.

As standard of care, pembrolizumab or palliative radiotherapy are routinely given (as it would be in this study), but not in this special combination. Instead of being in this study, you can choose to be treated with pembrolizumab, without the addition of radiation treatment, or you can choose to be treated with palliative radiotherapy, without the addition of pembrolizumab. If you choose not to be a part of this study, you may still be treated with radiotherapy with the goal of relief of cancer-related symptoms, if necessary. You may also receive pembrolizumab, but not in combination with the radiation like in this study.

WHAT ARE THE COSTS?

For patients with recurrent, advanced or metastatic head and neck cancer, pembrolizumab immunotherapy is a standard of care. The radiation treatments are often used for patients with this kind of cancer in order to control symptoms caused by the tumor in the head and neck area. This type of treatment is very often covered by the medical insurance. However, taking part in this study may lead to added costs to you or your insurance company. We will give you an estimate of what the added cost may be based on your particular situation and insurance coverage.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

WILL YOU BE PAID FOR PARTICIPATING?

Parking will be validated for all study-related visits.

You will receive no payment or other compensation aside from parking validation for taking part in this study.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Health Sciences. The researchers do not hold a direct financial interest in the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Mercedes Porosnicu at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** Demographic information, history of tobacco and alcohol use, medical history, physical exam, performance status assessment, vital signs, height, weight, EKG, current medications, and tumor imaging by CT

scan or MRI, PET scan.

Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.
Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

Some of the people, agencies and businesses that may receive and use your health information are investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state

privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Porosnicu that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Mercedes Porosnicu, MD
Section on Hematology and Oncology
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH

medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Mercedes Porosnicu at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the

sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm