A Single Arm Phase II Study of

Cemiplimab-rwlc in Immunocompromised Patients with Unresectable Locally Recurrent and/or Metastatic Cutaneous Squamous Cell Carcinoma (CSCC)

NCT04242173

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CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Study Title:	**A Single Arm Phase II Study of Cemiplimab-rwlc in Immunocompromised Patients with Unresectable Locally Recurrent and/or Metastatic Cutaneous Squamous Cell Carcinoma (CSCC)**
Protocol Number:	**MCC 20114**
Sponsor:	**Moffitt Cancer Center**
Principal Investigator: (Study Doctor)	**Christine H. Chung, MD**
Telephone: (24 hour number)	**813-745-5061** **800-456-3434**
Address:	**Moffitt Cancer Center** **12902 Magnolia Drive** **Tampa, FL 33612** **Moffitt Cancer Center McKinley** **10920 N. McKinley** **Tampa, FL 33612**

You are being asked to take part in a research study. The information in this document should help you to decide if you would like to participate.

The purpose of this research study is to determine how people with weakened immune systems and unresectable (cannot be removed by surgery) locally recurrent and/or metastatic cutaneous squamous cell carcinoma (CSCC) respond to study treatment with Cemiplimab. Cemiplimab is approved for sale in United States by the U.S. Food and Drug Administration (FDA). About 27 participants will participate in this study.

During the study, you will receive Cemiplimab study treatment that will be administered every 21 days for approximately 1 year (17 cycles). Each study treatment will be administered intravenously for approximately 30 minutes. You will stop receiving study treatment prior to 1 year if your disease progresses, you experience intolerable side effects, or you withdraw your consent for study participation.

Some of the most common side effects of Cemiplimab include fatigue, nausea, diarrhea, constipation, decreased appetite, and rashes. Cemiplimab can also cause side effects called immune-related adverse reactions. These side effects can be serious and require corticosteroid treatment or discontinuation of the study medication. Some examples of these immune-related

side-effects are pneumonitis (inflammation of the lung), colitis (inflammation of the colon), and hepatitis (inflammation of the liver). Please see the "ARE THERE RISKS TO ME IF I AM IN THIS STUDY" section of this form for additional immune-related side effects. Other potential serious side effects include, but are not limited to, diabetic ketoacidosis (a potentially dangerous buildup of acids in your blood), damage to the liver, infusion related reactions, and Guillain-Barre Syndrome (damage to the nervous system). Please review the "ARE THERE RISKS TO ME IF I AM IN THIS STUDY?" section of this form for additional information on Cemiplimab side effects.

In addition to receiving the study drug, throughout the study you will visit the clinic and undergo the following procedures: you will be asked questions about your medical history and any medications you are currently taking; you will be asked questions about any symptoms you may be experiencing; you will complete physical exams and your vital signs will be assessed; you will complete laboratory tests; you will complete a pregnancy test, if applicable; you will undergo imaging studies (CT/MRI); and you may provide an optional tumor biopsy. Additional information about the study procedures can be found in the "WHAT WILL HAPPEN DURING THIS STUDY?" section of this form.

Your participation is voluntary, and you may stop your participation at any time. There will be no penalties or loss of benefits or opportunities if you do not participate or decide to stop once you start. Any new important information that is discovered during the study which may influence your willingness to continue participation will be provided to you.

We do not know if you will receive any benefit from your participation. There is no cost to participate. You will not be compensated for your participation.

Even if we publish the findings from this study, we will keep your study information private and confidential. Anyone with the authority to look at your records must keep them confidential.

WHAT IS THIS STUDY ABOUT?

You are being asked to participate in this research study because you have a weakened immune system and unresectable (cannot be removed by surgery) locally recurrent and/or metastatic cutaneous squamous cell carcinoma (CSCC).

The purpose of this research study is to:

- test the safety and effectiveness of the study drug, Cemiplimab.

This research study will test the investigational drug, Cemiplimab. Cemiplimab is approved by the United States Food and Drug Administration (FDA) for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. This study is designed to test the safety of Cemiplimab and to see how your type of cancer responds to Cemiplimab study treatment in participants with weakened immune systems.

WHAT WILL HAPPEN DURING THIS STUDY?

Screening:

Before any study-related tests and procedures are performed, you will be asked to read, sign and date this consent document. The following screening tests and procedures will then be performed to determine if you qualify to take part in this study:

- You will be asked questions about your medical history
- You will be asked questions regarding any symptoms you may be having
- You will be asked questions about your daily activities
- Your vital signs will be taken
- You will complete a physical exam
- Blood will be collected for laboratory tests
- You will complete a pregnancy test, if applicable
- You will complete a computed tomography (CT)/magnetic resonance imaging (MRI) scan of the head/neck/chest/abdomen/pelvis and other areas where your cancer is. You may also have photographs taken of your cancer, if visible.
- You will provide an archived tumor sample (tissue from a previous biopsy or surgery)
- You will be asked to provide an optional, new tumor biopsy sample
- You will be asked about any medications you may be taking
- You will provide demographic information (such as age, gender, etc.)

If you qualify to take part in this study and go on to receive the study treatment then the following will happen:

Study Treatment:

You will receive Cemiplimab every 21 days for approximately 1 year (17 cycles). Each study treatment will be administered intravenously (directly into your vein) for approximately 30 minutes. You will stop receiving study treatment prior to 1 year if your disease progresses, you experience intolerable side effects or you withdraw your consent for study participation. Because this is a research study, the study drug will be given to you only during this study and not after the study is over.

During the study treatment portion of the study, you will continue to come to the clinic for study visits and undergo the following procedures:

- You will complete physical exams
- Your vital signs will be taken
- Blood will be collected for laboratory tests
- You will complete CTs/MRIs of the head/neck/chest/abdomen/pelvis and other areas where your cancer is. You may also have photographs taken of your cancer, if visible.
- You will be asked about any medications you are taking
- You will be asked about any symptoms you may be experiencing

End of Study Treatment Visit:

An end of study treatment visit will be performed once you end the study treatment period for any reason (your disease progresses, you have harmful side effects, or if you with withdraw your consent to participate in the study). This visit will take place approximately 30 days after your last dose of Cemiplimab. During this visit, the following procedures will be performed:

- You will complete a physical exam
- Your vital signs will be taken
- Blood will be collected for laboratory tests
- You will be asked about any medications you may be taking
- You will be asked about any symptoms you may be experiencing
- You will be asked to provide an optional, new tumor biopsy sample
- You will complete a CT/MRI of the head/neck/chest/abdomen/pelvis and other areas where your cancer is. You may also have photographs taken of your cancer, if visible. If you have had these procedures performed recently, it may not be necessary to repeat.

Final Study Visit:

At the end of the study (about 24 months after your first dose of Cemiplimab) you will complete a final study visit. During this visit, the following procedures will be performed:

- Blood will be collected for research purposes

Follow-Up Study Visits:

You will return to the study clinic approximately 6 months and 12 months after your end of treatment visit for a physical exam and laboratory tests

Additional information on the required study procedures can be found below:

- **Demographic Questions:** you will be asked to give personal information, such as your name, date of birth, and race.
- **Health and Medication Questions:** you will be asked to answer questions about your health, your medical history, and the medications you take.
- **Physical Exam:** a comprehensive physical exam, including a neurological evaluation, will be performed. You should ask you study doctor to explain what will happen during this exam.
- **Vital Signs:** the study team will check your blood pressure by putting a band around your arm (this will squeeze your arm for about a minute), check your pulse, listen to you breathe in and out, and will take your temperature. Your height and weight will also be assessed.
- **Blood Testing:** blood will be collected for laboratory tests
    - Some of your blood will be used to check on your health.
    - Some of your blood will be used for research purposes.
- **Pregnancy Testing:** a blood or urine test will be performed to see if you are pregnant. You will only have pregnancy testing if you are a woman and can have children. The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.
- **CT Scan:** A CT scan uses radiation (x-rays) to make pictures of the inside of your body. The scan can show a cross-section (a thin “slice”) of your body, or can show the body tissues and structure in 3 dimensions (“3-D”). The study doctor or study staff may give you a contrast dye, either by mouth or with a needle. The study doctor can tell you more about contrast dye.
- **MRI:** An MRI uses powerful magnets and radio waves to make pictures of body tissues and structure.

- **Optional Biopsies:** If you agree, a tissue sample will be collected, prior to receiving the study drug (during the screening portion of the study) and at the end of the study. The information obtained from these samples will be used for future research of your disease. You do not have to provide the samples in order to participate in this study. You will be asked to provide your consent to the optional biopsies at the end of this consent form.

HOW WILL MY SAMPLES BE USED?

In addition to the procedures outlined above, we are asking you to allow us to store your optional tumor biopsies and blood samples, collectively referred to as "tissue", for use in future research. These samples may be used for research on your disease or condition and others to assist in the development of new treatments.

In addition to your samples being used for this study and future research, we would like to share them with other researchers. We will code your samples so that the researcher who uses it for other purposes does not know your identity. We will not release the code that links your sample to your personal identifying information for any reason.

This study also involves genetic testing. Genes control how your body grows and changes, and how your body reacts to certain things. Genes are what we get from our parents that help make our bodies what they are. For example, eye and hair color depend on the genes we received from our parents. We want to find out how genes work in skin cancer. It may be true that some people are more likely to have skin cancer because of their genes and we would like to learn more about this.

As part of this study, a blood sample will be obtained and DNA from your blood sample will be purified. DNA, or deoxyribonucleic acid, stores and transmits inherited traits, such as eye color or blood type. As part of this research project, your DNA will be studied in an effort to find out if there are genes that contribute to medical conditions that are part of this study.

We will not tell you what we find out about your genes. For example, we might find out that you have a certain kind of gene. We may know that if people have this gene, they sometimes get a certain disease or do not respond to treatment. You could have a gene that makes it more likely that you will have a health problem. However, that does not mean you will get that health problem. You should ask the study team or a genetic counselor if you have any questions about genetic research.

Your sample will be stored with your name or other identifying information and health information linked to it. We will not share your name or other information that identifies you unless it is required by law. Since your genetic sample is linked to identifying information, should you choose to withdraw your consent to use the sample at a later date, please contact the study team. The study team will remove your sample from the research and immediately destroy it so that it can no longer be used. Please understand that part of your sample may have been used prior to the withdrawal of your consent.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading", every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research will include whole genome sequencing (i.e.,

sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

As part of the genetic study, a sample of your DNA may have Genome Wide Association Studies (GWAS) performed. This analysis creates a very detailed picture of your DNA for researchers. In addition, information regarding your DNA and clinical information about you will be sent to the National Institute for Health's Genome Wide Association Study (GWAS) data repository, where it will undergo genome-wide analysis and be shared with other investigators for research purposes. DNA and information sent to the GWAS database will help researchers better understand how genes affect the risk of developing diseases and may lead to better methods to select the best treatment options. Before your information is sent to the GWAS data repository it will be de-identified, which means that we will remove any identifying information such as your name, date of birth, address, etc. Thus, researchers using your DNA and clinical data will not be able to link this information back to you.

Genetic Information Nondiscrimination Act (GINA)

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), 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.

All health insurance companies, group health plans, and employers as outlined above must follow this law. Please note that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

WHO IS PAYING FOR THIS STUDY?

A company called Regeneron Pharmaceuticals, Inc., the manufacturer of the study drug, is paying for this study.

WILL IT COST ANYTHING TO BE IN THIS STUDY?

You and/or your insurance company will be financially responsible for hospital inpatient, outpatient and follow-up visits that would normally or routinely occur in the management of your disease. Inpatient and outpatient visits could include charges for treatments, medications, physician visits, laboratory tests and procedures. You and /or your insurance company will be responsible for paying for the charges which are considered routine, since you would have received these services even if you were not participating in this study. You will be responsible for any costs not covered by your insurance company, including deductibles, co-payments and

all out-of-pocket expenses. Before you agree to be in this study, you should contact your health insurer to see if your plan will cover the costs required as part of your participation.

You and/or your insurance company will not be responsible for paying for study related items and services that are specifically required for this research study and are not considered part of the routine management of your disease, if these procedures are performed at Moffitt Cancer Center.

During your participation in this study, the study sponsor will be responsible for providing the study drug, Cemiplimab, at no additional charge to you. You and/or your insurance company will be responsible for the charges related to the administration of the study drug.

If you would like more information on the costs of being on this study or have other insurance related questions then please let your clinical trial coordinator know or contact our Business Office at 813-745-8422.

WILL BEING IN THIS STUDY HELP ME?

You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Information learned from the study may help other people in the future.

ARE THERE RISKS TO ME IF I AM IN THIS STUDY?

The Cemiplimab might not help.

Right now, we do not know for sure if Cemiplimab will help. If it does not help, your condition/disease may get worse.

You may have problems because of the Cemiplimab. These problems are called side effects. Some side effects are just bothersome. Others could harm you. There may be some side effects that we do not know about yet. The research might involve risks to you that are currently unforeseeable. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study drug. In some cases, side effects can be serious, long lasting, or may never go away. There may also be the risk of death.

HERE ARE THE KNOWN SIDE EFFECTS THAT COULD HAPPEN WITH CEMIPLIMAB

Risks and side effects related to the Cemiplimab include those which are:

Most Common (more than 10% of participants)

- Fatigue (tiredness)
- Rash

Common (1 to 10% of participants)

- Nausea (feeling sick to your stomach)
- Diarrhea

- Arthralgia (joint pain)
- Itchiness
- Damage to the liver (from inflammation) that causes an abnormal result on a blood test of liver function and may cause symptoms
- Underactive or overactive thyroid gland (which can cause tiredness, constipation, hair loss, sensitivity to heat or cold temperatures, mood changes, sweating, muscle aches, a fast heartbeat or weight changes)
- Decreased appetite
- Fever
- Infusion-related reaction
- Myalgia (muscle pain)
- Asthenia (weakness or lack of energy)
- Chills
- Pneumonitis (inflammation of the lung) which may be life-threatening or may lead to death
- Vomiting
- Dry mouth
- Headache
- Dry Skin
- Cough
- Stomatitis (inflammation of mouth and lips)
- Anemia (low red blood cells that can cause tiredness, physical weakness or lack of energy)
- Abdominal (stomach) pain
- Dizziness
- Constipation
- Flu-like illness
- Insomnia (trouble sleeping)
- Shortness of breath
- Low white blood cells (that can make it more likely to get an infection)
- Swelling of arms or legs
- Blood creatinine increased which indicates impaired kidney function or kidney disease

Rare and serious (less than 1% of participants)

- Encephalitis (inflammation of the brain) which may result in severe memory loss and occasionally death.
- Myasthenia gravis, a disease that causes muscle weakness
- Colitis, an inflammation of the colon
- Diabetic ketoacidosis, a severe complication of diabetes (high blood sugar) where the body makes too much acid in the blood
- Diabetes mellitus
- Hypophysitis, pituitary gland inflammation (possible headaches)
- Myocarditis, inflammation of the heart muscle

- Meningitis, inflammation of the membrane around the spinal cord and brain (possible headache and/or coma)
- Guillain-Barre syndrome, damage to the nervous system (causing numbness and/or paralysis)
- Pancreatitis, inflammation of the pancreas causing pain in the upper abdomen. This could become severe and cause nausea and vomiting, fever and rapid heart rate
- Pemphigoid, large skin blisters
- Adrenal insufficiency/Adrenocorticotropic hormone deficiency: Adrenal gland does not produce enough of certain hormones
- Pericarditis: inflammation of the pericardium which is two thin layers of a sac-like tissue that surround the heart
- Myositis: inflammation of the muscles

Cemiplimab can cause some type of side effects called immune-related adverse reactions. These immune-related side effects can be serious and require corticosteroid treatment and interruption or discontinuation of study treatment. It is important to contact your study doctor immediately if you experience any of these symptoms described below or if they get worse:

- Pneumonitis (inflammation of the lung): new or worsening cough, chest pain, or shortness of breath.
- Colitis (inflammation of the colon): diarrhea, blood in stool or severe abdominal pain
- Hepatitis (inflammation of the liver): jaundice (yellowing of skin, mucus membranes or whites of eyes), severe nausea or vomiting, or easy bruising or bleeding
- Hypophysitis (inflammation of pituitary gland which secretes hormones to control several body processes): persistent or unusual headache, extreme weakness, dizziness or fainting, vision changes, or other changes due to an effect on your hormones
- Nephritis (inflammation of the kidney): pain in pelvis, pain or burning during urination, frequent urination, blood in urine, vomiting, fever
- Hyperthyroidism and Hypothyroidism (over or underactive thyroid gland): tiredness, weight gain or loss, hair loss, constipation, depression, irritability, muscle aches, intolerance to heat or cold
- Uveitis (inflammation of the eye): eye redness, eye pain, light sensitivity, blurred vision, floaters, decreased vision
- Skin changes: peeling of the skin over large areas of the body, rash, itching, skin blistering.
- Mucositis (painful inflammation and ulceration of mucous membranes lining the digestive tract): painful sores in the mouth, tongue, nose or throat which can make it hard to eat or drink
- Encephalitis (inflammation of the brain): headache, fever, tiredness, confusion, memory problems, sleepiness, seeing or hearing things that are not really there, seizures, stiff neck

ALTERNATIVE TREATMENTS

Some potential alternatives to participating in the study are palliative chemotherapy or cetuximab.

As with any medication or chemotherapy treatment, there may be risks, known and unknown.

The most common temporary side effects for **some** chemotherapy drugs may include nausea and vomiting, loss of appetite, hair loss, mouth sores, higher risk of infection (due to decreased white blood cells), bruising or bleeding, fatigue (feeling tired), and changes in your menstrual cycle if you are a woman, (such as, irregular periods or symptoms of menopause [end of menstruation]).

A more complete listing of side effects for other therapies may be available for you to review if you wish. Please talk with your study doctor about the risks of both this investigational drug and any alternative methods of treatment that are available.

WHAT CAN HAPPEN IF I GET INFUSIONS?

The study doctor will give you the study drug by sticking a needle in your skin. Some problems you might have from this are:

- Pain
- Bruising
- Dizziness
- Infection

You will receive the study drug intravenously, which means you will receive it directly into your vein. This may cause the following problems:

- Irritation of the vein; your skin near the vein could become warm, swell, hurt, or get red
- Damage to your vein
- Damage to the skin or tissue around the injection site
- Too much of the study drug may be given to you
- An increase or decrease in electrolyte levels (the amount of certain salts and other chemicals in your blood), could occur which could cause health problems
- A blood clot or an air bubble could form, which could block a blood vessel in another part of your body

Some of these problems could be very serious.

Over time, getting a lot of injections can cause a vein to become hard or scar, which can make it difficult to put a needle into the vein to give you a shot or take blood.

COULD I HAVE AN ALLERGIC REACTION?

Occasionally, people have allergic reactions to medications which may require medical treatment. A severe allergic reaction could be life-threatening. Examples of an allergic reaction include: a rash; shortness of breath; wheezing; difficulty breathing; sudden drop in blood pressure; swelling around the mouth, throat, or eye; fast pulse; and sweating. You should get

immediate medical help and contact the study doctor if you have any of these or any other side effects during the study.

IS THERE ANY RISK TO YOUR UNBORN CHILDREN IF YOU TAKE PART IN THIS STUDY?

FOR WOMEN:

If you are pregnant, you cannot participate in this study, because there may be risks to you and your unborn baby that are currently unforeseeable; risks that we do not know about yet. Breastfeeding (nursing) mothers will not be included in this study, since it is not known whether the study drug will be passed on to the baby in mother's milk. If you are currently breastfeeding and wish to continue breastfeeding, your study doctor may recommend another treatment.

If you are a woman of childbearing potential (able to become pregnant), you will be given a pregnancy test before beginning any study drug.

Tell the study doctor right away if:

- You are pregnant.
- You become pregnant.
- You are planning to become pregnant.
- You are breastfeeding.

FOR MEN AND WOMEN:

Whether you are a man or a woman, there may be risks to your unborn children that we don't know about ahead of time; they are unforeseeable.

If you take part in this study, you must use an effective birth control method as discussed with your study doctor and continue to use it until at least 6 months after your last dose of study drug.

Examples of birth control methods include:

- Oral birth control pills
- Birth control patch
- Implanted (injectable contraceptive hormones or mechanical products such as intrauterine device)
- Barrier methods (such as: diaphragm, condoms, or spermicides)
- Tubal ligation or vasectomy
- Abstinence (no sexual intercourse)

You should discuss the method of birth control which is best for you to use both during study treatment and for a period of time after study treatment.

Whether you are a woman or a man, you should tell your study doctor immediately if you become pregnant or if your partner becomes pregnant. Women who become pregnant during the study will have to leave the study.

The long-term effects of the study drug on fertility are unknown. This means that it is unknown if the study drug will affect your ability to have children in the future. If we find out that the study drug might harm your fertility, you will be informed.

Cancer treatment can affect fertility in both men and women, and it is important to understand the risks before starting study therapy. Ask your study staff about fertility preservation before you begin study treatment. However, once you have started study treatment you should not donate or sell your eggs or sperm.

COULD I HAVE ANY OTHER PROBLEMS WITH MY HEALTH IF I DO THIS RESEARCH STUDY?

It is possible that you could have problems and side effects of Cemiplimab that nobody knows about yet, which include your cancer getting worse or even death. If the study doctor learns any new

information that might change your mind about continuing in the study, the study doctor or study staff will tell you about it. The study doctor will also tell you if new treatments become available for your cancer.

It is possible that taking Cemiplimab with your regular medications or supplements may change how, the study drug or your regular medications, or regular supplements work. It is very important that you tell the study doctor about all medications or supplements you are taking during the study.

WHAT ARE THE RISKS OF GIVING BLOOD FOR THIS STUDY?

Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

You will give about 20 ml (4 teaspoons) of blood for research purposes at screening, at the start of cycles 3, 6, 9 and 12, at End of Study Treatment (EOST), and End of Study (2 years after your first study treatment). In total, this will amount to approximately 140 ml (about 9 tablespoons) of blood.

WHAT ARE THE RISKS OF HAVING A BIOPSY DONE FOR THIS STUDY?

Optional Tumor Biopsy

Risks of a tumor biopsy are localized bleeding at the needle injection site or from the surgical incision, pain, inflammation, swelling, and infection. The bleeding may cause discomfort and bruising. In rare circumstances (less than 1%), this bleeding may be severe enough to require further care. If you have a history of excessive bleeding, or if you are receiving medication that might increase your risk of bleeding (such as aspirin or blood thinners), you must notify the study doctor before the procedure. Infection of the surgical site may require treatment with antibiotics.

Tumors that are biopsied from the lungs may result in an additional risk of pneumothorax (collapsed lung). Biopsies in or near other vital organs may result in bleeding that can be life-threatening or may cause damage to the organs and affect their function.

Depending on the site, the biopsy procedure may use local anesthetics (numbing medicine), sedatives, or general anesthesia to reduce the discomfort or pain. All medicines have the

possible risk of allergic reaction. Please advise your study doctor if you have ever had an allergic reaction to latex, lidocaine, or any other anesthetic.

Any complications arising from the biopsy may be treated with observation, additional medications, or in some cases, additional surgery. The study doctor will discuss the specific risks of the biopsy with you at the time of the procedure.

Liver Biopsy

For participants undergoing an optional liver biopsy, there may be increased risk in certain circumstances. When study doctors perform your liver biopsy, they do so by passing a needle into the liver usually through your side. Doctors are usually able to get a large enough piece of liver to examine under the microscope by taking a single biopsy of the liver. However, in some participants, only a small piece is retrieved (not enough to look at under the microscope) and in this case, a second specimen from the liver is taken for clinical diagnosis. However, after the first attempt, if there is enough for clinical purposes, but not for research purposes, a second piece will be taken for research purposes. Thus, by participating in this study, in a small fraction of participants undergoing liver biopsy (less than 5% of all participants), there will be a chance that a second piece of liver will be taken for research purposes. The additional risk of an additional liver sampling is approximately 1 in 1,000 for increased bleeding, and 1 in 2,000 for other complications such as puncture of a lung or colon. These complications are managed by observation and, in some circumstances, surgery.

Skin Biopsy

A skin biopsy is generally a non-hazardous procedure; however, possible hazards may include: 1) reaction to anesthetic (numbing medicine), 2) excessive bleeding, 3) bruising, 4) infection and 5) excessive scarring. While the local numbing medicine xylocaine is almost entirely free from allergic properties (such as causing hives), an allergic reaction is possible, and you will not be given xylocaine if you have a history of such a reaction. The xylocaine will be given by a small injection into the skin at the site of the skin biopsy. To speed healing, one or two stitches (also known as sutures) will be placed, which will be removed 5 - 7 days later. During the healing process, you will be asked to keep the biopsy site clean and dry, and to apply antibiotic ointment. Infection rarely occurs and is largely prevented by the use of an aseptic (or sterile) biopsy technique and proper wound care. If infection does occur, you will be instructed to keep the wound clean and to apply warm, wet compresses for 15 minutes, three times a day, until the infection subsides. If the infection persists, antibiotics may be prescribed.

Only 10-15 minutes will be required for the biopsy procedure. After the anesthesia wears off, there will be some soreness at the biopsy site that will last for a few hours. A small scar will develop at the site of the biopsy.

WHAT ARE THE RISKS OF OTHER STUDY PROCEDURES?

MRI

Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will ask you about metal within your body, including medical implants, devices such as

pacemakers and internal defibrillators, or certain dyes found in tattoos. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner.

If there is any question about potentially hazardous metal within your body, you will not undergo the MRI. This may exclude you from participation in this research study. The MRI involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. You will hear a loud machine-like noise. You may be asked to have a harmless monitoring device applied during the MRI. During the MRI, you can have voice contact and physical contact with someone in attendance if you desire. Let the study doctor know if you have a fear of enclosed spaces.

CT Scan

Computed Tomography (CT) is a way to make x-ray images of the inside of the body. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures that show structures inside your body more clearly than regular x-ray pictures. During the procedure, a technologist will take you into the CT scan room where you will lie down on the table (usually on your back) inside of the CT machine. You should get comfortable because it is very important that you not move during certain parts of the test.

CT examinations differ depending on the part of your body being studied. For example, if your abdomen is being studied, a series of pictures will be taken from your lower chest to your lower pelvis. During the study, you will be asked to hold your breath so that the pictures will not be blurred. The machine will make some noise, and the table will move during the scan. Also, you may receive signals from the technologist or from the machine about your breathing. Before or during the study, you may be given an injection of a contrast liquid in your vein to allow the radiologist to obtain clearer images of your organs. If you have any discomfort during the test or after the injection, be sure to tell the technologist.

Confidentiality

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

WHAT IF I GET HURT OR SICK WHILE I AM IN THIS STUDY?

If you need emergency care:

- Call 911 or go to your nearest emergency room right away. Moffitt Cancer Center does not have an emergency room or the facilities to provide emergency care.

If you do NOT need emergency care:

- Call or go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

If you experience a side effect or a change in the way that you feel, call the study doctor at the telephone number listed on the first page of this form.

By signing and dating this informed consent and research authorization form, you have not given up any legal rights to seek compensation for injuries from the sponsor**.**

MOFFITT CANCER CENTER INJURY STATEMENT

If you believe you have been injured as a result of your participation in this study or if you have questions about your rights as a person who is taking part in a research study, you may call the Moffitt Cancer Center Risk Manager at 813-745-7882. Moffitt Cancer Center and its investigators have made no provision for monetary compensation in the event of physical illness or injury resulting from this study. Likewise, Moffitt Cancer Center and its investigators have made no provision for payment of lost wages, disability, or discomfort in the event of physical illness or injury resulting from this study. Florida law (Statute 768.28) limits the liability of Moffitt Cancer Center. This statute provides that damages are available only to the extent that negligent conduct of a Moffitt Cancer Center employee caused your injuries, and are limited by law.

WILL I GET PAID?

You will not get paid for being in this study. You will not be reimbursed for expenses for travel and/or lodging while taking part in this study.

WHILE YOU ARE IN THE STUDY, YOU MUST:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor.
- Give correct and accurate information about your medical history and current medical condition.
- Tell the study doctor about any health problems you have during the study.
- Tell the study doctor about any new medicine or drug you take during the study.
- Not take any other drugs or remedies unless the study doctor has approved them beforehand. This includes prescription drugs and over the counter medicine (including vitamins and herbal remedies) that you buy without a prescription.
- Not participate in other medical research studies.
- Not get pregnant or cause your partner to become pregnant.
- Tell the study doctor or study staff if you want to stop being in the study at any time.

DO I HAVE TO REMAIN ON THIS STUDY ONCE I JOIN?

If you want to stop being in the study, tell the study doctor or study staff. If you stop being in the study early, the study doctor or study staff may ask you some questions about being in the study. To help you leave the study safely, the study doctor may ask you to participate in more tests or return for a final study visit.

ARE THERE REASONS THE STUDY DOCTOR OR SPONSOR MIGHT TAKE ME OUT OF THE STUDY LATER?

Even if you want to stay in the study, there may be reasons the study doctor or study staff will need to take you out of it. Your study doctor has the right to take you out of the study at any time with or without your agreement. Your participation may be ended without your consent for different reasons, including the following:

- If the study doctor believes, for any reason, that it is in your best interest.
- If at any time while you are taking the study drug the study doctor discovers that your disease has worsened.
- If you develop side effects that the study doctor considers unacceptable.
- If you refuse to take the study drug or return for follow-up as recommended by your study doctor, or do not follow the study doctor's instructions.
- If you refuse to have tests that are needed to determine whether the study drug is safe and effective.
- If you require treatment with drugs that are not allowed on this study.
- If other causes prevent you from continuing in this study.
- If the Sponsor decides to end the study.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment and because of federal law, we must obtain your written authorization before we use or disclose your information for this study.

By signing and dating this form, you are permitting researchers at Moffitt Cancer Center to use personal health information for research purposes within its organized health care arrangements. You are also allowing the Moffitt Cancer Center to disclose your personal health information to outside organizations or individuals that participate in this study. We may publish what we find out from this study. If we do, we will not let anyone know your name. We will not publish anything that would directly let people know who you are.

Identifiers might be removed from your identifiable private information or identifiable biospecimens collected during this study and could then be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

WHO WILL DISCLOSE, RECEIVE, AND/OR USE YOUR INFORMATION?

Your records are confidential and they will be kept in a secure environment and protected to the full extent of the law.

To do this research, the following people and/or organization(s) will be allowed to disclose, use, and receive your information, but they may only use and disclose the information to the other parties on this list, to you or your personal representative, or as permitted by law:

- Every research site for this study, including the Moffitt Cancer Center, and each site's study team, research staff and medical staff.
- Any person who provides services or oversight responsibilities in connection with this study.
- Every member of the Moffitt Cancer Center workforce who provides services in connection with this study.
- The person who is responsible for the study nationwide or worldwide (study chairperson).
- Any laboratories, individuals, and organizations that use your health information in connection with this study.
- Any funding source of the study, including Regeneron Pharmaceuticals, Inc.
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA) and Florida Department of Health (FDH). The U.S. Department of Health & Human Services (DHHS), Office for Human Research Protections (OHRP).
- Other government agencies in this or other countries.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards such as Advarra IRB, Privacy Boards, Data and Safety Monitoring Board and their related staff that have oversight responsibilities for this study.
- The National Cancer Institute in evaluating the ongoing research of the Moffitt Cancer Center as a Comprehensive Cancer Center.

The organizations and people listed above may employ or pay various consultants and companies to help them understand, analyze and conduct this study. All of these people may not be known now, but if you would like to have more specific information about this at any time during the study, you may ask the study doctor and your questions will be answered.

Moffitt Cancer Center cannot guarantee the privacy of your information, or block further use or distribution, after the information has left the Moffitt Cancer Center. Others listed above may further disclose your information, and it may no longer be covered by federal privacy regulations. If all information that does or can identify you is removed from your records, the remaining information will no longer be subject to this authorization and may be used or shared for other purposes. You might have the right to see and copy your health records related to this research. You might not be able to see or copy some of your records until after all participants finish the study. If it is necessary for your care, your records will be provided to you or your regular doctor.

WHAT INFORMATION WILL BE USED OR DISCLOSED?

By signing and dating below, you authorize the use and disclosure of your entire study record and any medical or other records held by Moffitt Cancer Center, including, but not limited to, HIV/AIDS, mental health, substance abuse or genetic information. The purpose for the uses and disclosures you are authorizing is to conduct the study explained to you during the informed consent and research authorization process and to ensure that the information relating to that study is available to all parties who may need it for research purposes.

Your authorization to use your health information will never expire unless and until you expressly revoke it in writing to the study doctor listed on the first page of this form.

Any data collected before your letter will continue to be used as necessary to preserve the integrity of the study, however no additional information will be collected after you withdraw your authorization.

You will receive a signed and dated copy of this form.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Participant Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Participant Adviser: Pro00037712.

WHERE CAN I GET MORE INFORMATION?

You may call the National Cancer Institute's (NCI) Information Service at:
1-800-4-CANCER (1-800-422-6237).

Visit the NCI's Websites at:

- CancerTrials: comprehensive clinical trial information at: http://cancertrials.nci.nih.gov
- CancerNet: accurate cancer information including PDQ at: http://cancernet.nci.nih.gov

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.

CONSENT FOR OPTIONAL TUMOR BIOPSIES

Participant's Initials _____ **Yes**, I agree to the optional tumor biopsies outlined in this consent form (1 to be performed at screening and 1 to be performed at the end of the study) and for the use of my biopsy samples in future research.

Participant's Initials _____ **No**. I do not agree to the optional tumor biopsies.

STATEMENT OF CONSENT AND AUTHORIZATION

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records.

_____

Printed Name of Participant

_____

Signature of Participant Date Time

STATEMENT OF PERSON OBTAINING INFORMED CONSENT / RESEARCH AUTHORIZATION

I attest that the participant named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Printed Name of Person Explaining Consent

_____

Signature of Person Explaining Consent Date Time