VUMC Institutional Review Board
Informed Consent Document for Research

Study Title: Phase 1/2 Study to Evaluate the Safety and Preliminary Activity of Nivolumab in Combination with Vorolanib in Patients with Refractory Thoracic Tumors.
Version Date: September 8, 2020
PI: Katy Beckermann, PhD, MD NCT03583086

Name of participant:_____ Age:_____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

What is the purpose of this study?

You are being asked to participate in this research study because you have been diagnosed with Non-Small Cell Lung Cancer (NSCLC), Small Cell Lung Cancer (SCLC), or Thymic Carcinoma. Your disease has not responded to standard therapy, or has returned or progressed after standard therapy; or no standard therapy is currently available for your disease.

The purpose of this study is to learn if the investigational drug called vorolanib can help your condition when used in combination with the immunotherapy drug nivolumab.

Investigational means vorolanib is still being tested in research studies and has not yet been approved by regulatory health authorities, such as the U.S. Food and Drug Administration (FDA). Vorolanib blocks new blood vessel growth to reduce the possibility of tumor growth.

Nivolumab (also known as OPDIVO®) and other anti-PD-1/PD-L1 drugs are approved by the FDA to be used alone for the treatment of patients with metastatic NSCLC whose cancer has spread after treatment with platinum-based chemotherapy. Drugs that block PD-1 or PD-L1 (these are proteins found in normal and cancer cells of your body) can help immune cells find cancer cells to attack them.

The addition of vorolanib to nivolumab may lead to increased side effects. There is the possibility that these side effects could require delays or lower doses of the scheduled study drug treatments. It is also possible that the combination of vorolanib and nivolumab may not offer an additional benefit compared to nivolumab alone.

Nivolumab increases the ability of the immune system to attack cells such as cancer.

This research study was developed at Vanderbilt University Medical Center (VUMC). Katy Beckermann, PhD, MD at the Vanderbilt-Ingram Cancer Center (VICC) is the sponsor-investigator of this study (also known as the study chair). This study will be conducted at Vanderbilt University Medical Center and up to approximately 4-6 other academic medical centers in the United States. Overall, up to approximately 177 patients are expected to enroll in this study.

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This study is partially funded by Equinox Sciences, LLC, which is affiliated with Xcovery Holdings, Inc. Equinox is the company that makes and is supplying vorolanib for use in this study. Equinox/Xcovery could benefit financially from this research study. This study is partially supported by Bristol-Myers Squibb. Bristol-Myers Squibb is the company that makes and is supplying nivolumab (Opdivo) for use in this study.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study. Anyone you authorize to receive your medical record will also get this note.

What will happen and how long will you be in the study?

If you qualify and agree to participate, your time in this research study will be followed in "Cycles". Each treatment Cycle lasts 8 weeks (56 days).

All patients enrolling in this study are scheduled to receive treatment with vorolanib and nivolumab:

- Vorolanib: Once every day.
- Nivolumab: Once every two weeks on Days 1, 15, 29 and 43 during each 8 week (56-day) treatment cycle for the first two treatment cycles. After which, the treatment schedule can change to every four weeks (i.e., on Days 1 and 29 of each 56-day cycle) if the patient is not exhibiting disease progression.
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Vorolanib is an oral drug, which you will take by mouth. You will take vorolanib with food, at about the same time each day, approximately 24 hours (± 2 hours) apart. You will write down when you take your vorolanib every day on a drug diary we will give you. Also, if you have a blood pressure cuff at home, you will be asked to take and record your blood pressure.

Nivolumab will be given by IV, infused into a vein in your arm (or similar site). Each nivolumab infusion is scheduled to take about 30 minutes. All patients are scheduled to receive the same dosage of nivolumab (240mg during each nivolumab infusion).

Dose Escalation: In the early part of the study (called Dose Escalation), approximately 9-18 total patients in groups of about 3-6 patients per group will receive increasingly higher doses of vorolanib. The purpose of Dose Escalation is to find the highest dose of vorolanib that does not cause unacceptable side effects when VOROLANIB is used in combination with nivolumab. You and your study team will know the dose of VOROLANIB that you will receive, but your study doctor cannot choose your vorolanib dose level. Thus, you may receive a dose of vorolanib that is higher or lower than other patients in the study.

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Dose Expansion: After the highest safe dose of vorolanib (called the maximum tolerated dose / MTD, or the recommended combination dose / RCD) is identified during Dose Escalation, the second part of the study (called Dose Expansion) will then use this dose of VOROLANIB to enroll up to about 90 total additional patients, in order to further examine the safety of vorolanib in combination with nivolumab, and to help initially understand if vorolanib + nivolumab does or does not work against Non-Small Cell Lung Cancer, Small Cell Lung Cancer and Thymic Carcinoma. In Dose Expansion, about 20-41 patients will enroll into each of the disease categories.

In this study we will look at genes (DNA) in your blood and tumor tissue to see how they affect health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment.

If you decide to participate in the study, you must first sign this consent form. Before you are treated, your study doctor will need to determine if you are eligible to take part in this study. By signing this form, you agree to follow the instructions given by the research staff during the study.

After reviewing and signing this consent form, you will be asked to undergo tests and procedures to find out if it is okay for you to take part in the research study. This is called screening. Some of these tests and procedures are likely to be part of the regular care you would receive even if you were not participating in the study. You may have had some of these tests or procedures recently done. If this is the case, these tests or procedures may not need to be repeated.

After these tests are reviewed, it is possible you will not be able to be in the study. There may be other reasons why you are unable to be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Side effects and risks that you can expect if you take part in this study:

This is the first time that vorolanib will be given in combination with nivolumab.

Therefore, there may be new side effects for vorolanib and nivolumab together in combination, which have not been reported for either drug when given alone. The study has been designed to monitor closely for side effects, but unexpected side effects are possible. The long-term effects of vorolanib and nivolumab are unknown.

As with any new drug exposure, there is a risk of allergic reactions that can be fatal. These reactions can start shortly after taking a new drug. Symptoms might include skin itching and redness, difficulty breathing and/or low blood pressure and may be severe in some cases.

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You may experience one or more of the risks indicated below from being in this study. Some risks described in this consent document, if severe, may cause death. In addition to these risks, there may be other unexpected and possibly severe, life-threatening or fatal side effects that could occur.

Tell your study doctor about any side effects you are experiencing and seek medical attention when necessary.

Risks of VOROLANIB

Based on findings in human patients who have taken vorolanib alone, risks of vorolanib may include the following:

Common (≥ 10%) risks of VOROLANIB may include:

- Diarrhea
- Nausea
- Vomiting
- Fatigue
- Hair color changes
- Rash
- Weakness
- Edema/ edema peripheral (fluid build-up, including in arms, legs, hands, and/or feet)
- Dysgeusia (altered sense of taste)
- Alanine and/or Aspartate aminotransferase increased (high levels of liver enzymes in the blood, which can indicate liver damage or injury).

Less Common (≤ 10%) risks of VOROLANIB may include:

- Anemia (low red blood cells, which could cause you to feel fatigued)
- Granulocytopenia (low numbers of granulocytes, a type of white blood cell; can increase the risk of infection)
- Leukopenia (low white blood cells, which can increase the risk of infection)
- Neutropenia (low numbers of neutrophils, a type of white blood cell; can increase the risk of infection)
- Thrombocytopenia (low platelets in the blood, which can increase the risk of bleeding)
- Dry eye
- Abdominal pain
- Ascites (extra fluid in the abdominal cavity, between the chest and the diaphragm)
- Constipation
- Dyspepsia (feeling of indigestion, burning, pain or discomfort in the upper abdomen)
- Dysphagia (difficulty swallowing)
- Gait disturbance (changes in the way you walk)

- Mucosal inflammation (oral or gastrointestinal mucositis), causing tenderness or pain in tissues like the inside of the mouth, or anus
- Blood creatinine increased (can indicate kidney stress or injury)
- Lymphocyte blood count decreased (can increase risk of infection)
- Waist circumference increased
- Weight increased or decreased
- Anorexia
- Decreased appetite
- Dehydration
- Hypertriglyceridemia (high levels of fatty acids; may cause shortness of breath, nausea, vomiting)
- Hypomagnesemia (low magnesium; may cause weakness, muscle cramps, irregular heartbeat, tremors, or confusion)
- Arthralgia (joint pain)
- Muscular weakness
- Muscle spasms
- Myalgia (muscle pain)
- Dizziness
- Headache
- Peripheral neuropathy (numbness, tingling and/or pain in the extremities)
- Parosmia (altered sense of smell)
- Proteinuria (protein in the urine, which can be a sign of kidney damage)
- Dyspnea exertional (shortness of breath during exercise)
- Epistaxis (nose bleed)
- Alopecia (hair loss, including possible eyelash/eyebrows)
- Dermatitis bullous (skin blisters)
- Dry skin
- Erythema (red patches on the skin)
- Hair growth abnormal
- Photosensitivity reaction (sensitivity to sunlight)
- Pruritus (itching)
- Rash erythematous (red rash)
- Urticaria (hives, or patches of skin with raised itchy bumps that are red or skin-colored)
- Hypertension (high blood pressure)
- Urinary retention (inability to completely empty the bladder)
- Increased cholesterol (LDL)
- Gingivitis
- Skin discoloration
- Palmar-Plantar erythrodysesthesia (hand-foot syndrome)

- Abnormal nails
- Dysphonia (difficulty speaking)
- Hypothyroidism
- Hypophosphatemia (low levels of phosphate)
- Hypocalcemia (low levels of calcium)
- Hyponatremia (low levels of sodium)
- Urinalysis abnormalities (increased white blood count)
- Increased bilirubin and GGT (gamma-glutamyl transferase)
- Cardiac arrhythmias (atrial, ventricular)
- QT prolongation (irregular heart rhythms)

Serious events considered related or at least possibly related to vorolanib have included:

- Acute pancreatitis (inflammation of the pancreas) symptoms of which include severe upper abdominal burning pain, nausea, and vomiting
- Deep vein thrombosis (DVT), a blood clot that forms in a vein deep in the body which can break off and travel through the bloodstream to an artery in the lungs, blocking blood flow (may be life threatening)
- Cerebral infarction (stroke), resulting may result in facial weakness and slurred speech; memory loss
- Fistula (unusual or abnormal connection between a tumor and an organ; usually a result of an injury or surgery)
- Pleural effusion (build-up of fluid around the lungs)
- Infections
- Pulmonary embolism (blood clot in a major blood vessel in the lungs), often caused by a blood clot in the legs or elsewhere in the body that travels to the lungs, causing sudden shortness of breath, or sharp chest pain worsened by coughing or taking a deep breath; without prompt treatment, can be life-threatening
- Low platelet count (which could increase the risk of bleeding)
- Hemorrhage (bleeding in the abdomen involving a tumor invading a major blood vessel), that could cause death
- Hypertensive crisis (severe increase in blood pressure that can damage organs) and acute pain (pain that begins suddenly)

In the body, one target of VOROLANIB is called the vascular endothelial growth factor receptor (VEGFR), which is involved in the growth of new blood vessels (angiogenesis). Currently, other drugs are FDA approved which also target VEGFR. Because VOROLANIB has similarities to these other drugs, it is possible that side effects seen in these other drugs may also be observed when patients take VOROLANIB.

The most common side effects (>20%) noted in at least one of the prescribing information labels for these approved drugs which are similar to VOROLANIB include:

- Fatigue
- Asthenia (weakness)
- Fever
- Diarrhea
- Nausea
- Mucositis/stomatitis (inflammation of mucus membranes; for example inside the mouth, which may appear red, inflamed and may bleed)
- Vomiting
- Decreased appetite/anorexia
- Weight loss
- Dyspepsia (feeling of indigestion, burning, pain or discomfort in the upper abdomen)
- Abdominal/ gastrointestinal pain
- Constipation
- Hypertension (high blood pressure)
- Peripheral edema (fluid build-up in the arms, legs, hands, and/or feet)
- Rash with or without skin peeling (desquamation)
- Hand-foot syndrome (reddening, swelling, numbness and peeling of skin on the hand palms and feet soles)
- Skin discoloration
- Dry skin
- Hair color changes
- Alopecia (hair loss)
- Altered taste
- Dysphonia (hoarse voice, or other difficulty speaking)
- Headache
- Back ache
- Musculoskeletal pain
- Arthralgia (joint pain)
- Myalgia (muscle pain)
- Extremity pain (pain in the arms, legs, hands, feet, fingers, and/or toes)
- Tumor pain
- Cough
- Dyspnea (shortness of breath)
- Bleeding.

Serious side effects previously seen with drugs similar to vorolanib include:

- Heart problems, such as reduced ability to pump blood (including decreased ejection fraction or congestive heart failure), impaired heart function and rhythm; or heart ischemia/infarction (heart attack)

- Liver damage or failure (hepatotoxicity)
- Thyroid dysfunction (imbalance in the thyroid hormones)
- Hemorrhage (serious bleeding, often requiring transfusion), including bleeding into the tumor
- Thrombosis / thrombotic / thromboembolic events (formation of blood clots in blood vessels), including a blood clot forming in a vein deep in the body (deep vein thrombosis / DVT) which can break off and travel through the bloodstream to an artery in the lungs (pulmonary embolism / PE) blocking blood flow (may be life threatening); tell your study doctor immediately about sudden shortness of breath, or sharp chest pain worsened by coughing or taking a deep breath; without prompt treatment, can be life-threatening
- Thrombotic microangiopathy (blood clots in small blood vessels that can affect the kidneys and other organs)
- Hand-foot syndrome (reddening, swelling, numbness and peeling of skin on the hand palms and feet soles)
- Severe rash or severe skin reactions that can be life-threatening (such as erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis)
- Serious infections, including necrotizing fasciitis (serious rapid skin infection often caused by bacteria; requires treatment to prevent wider damage or death of tissue)
- Hole in the intestine (gastrointestinal perforation), or an abnormal passage between an organ and other tissues (fistula), which can be caused by tumor shrinkage
- Osteonecrosis of the jaw (breaking down of the bone in the jaw)
- Proteinuria (protein in the urine, which can be a sign of kidney damage); if severe can cause swelling (nephrotic syndrome)
- Reversible posterior leukoencephalopathy syndrome (neurological changes associated with headaches, mental status changes and possible seizures)
- Tumor lysis syndrome (complications from rapid break down of tumor cells).

Based on studies in animals, potential risks of vorolanib may include:

- Changes to the adrenal glands (tissue above the kidneys which makes hormones), which could cause changes to levels of hormones in the blood such as steroids
- Lymphoid depletion (changes to / shrinkage of lymph nodes), which can indicate abnormal changes to the immune system
- Changes to the pancreas
- Bone marrow hypocellularity (can indicate a reduced ability to produce appropriate levels of cells needed to transport oxygen, clot the blood, and fight infection)
- Changes in red blood cell counts, hemoglobin, and hematocrit (can indicate reduced ability of the blood to properly transport oxygen to the body tissues)
- Lower white blood cell and absolute lymphocyte counts (can indicate a reduced ability to fight infections)
- Higher platelet counts in the blood
- Changes to blood levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and/or alkaline phosphatase (may indicate liver stress or damage, or bone problems)
- Changes to blood levels of creatine kinase (indicating possible damage to muscles, including the heart)

- Changes in blood concentrations of sugars, elements and minerals (such as glucose, calcium and potassium).

Risks of Nivolumab (also known as OPDIVO®)

The following information is provided in the FDA approved Prescribing Information (version dated August 2018) for nivolumab, also known as Opdivo®.

What is the most important information I should know about Opdivo?
Opdivo is a medicine that may treat your melanoma, lung cancer, kidney cancer, blood cancer, head and neck cancer, colon or rectal cancer, liver cancer, or bladder cancer by working with your immune system. Opdivo can cause your immune system to attack normal organs and tissues in many areas of your body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your study doctor right away if you develop any symptoms of the following problems or these symptoms get worse:

Lung problems (pneumonitis). Symptoms of pneumonitis may include:
- New or worsening cough
- Chest pain
- Shortness of breath.

Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include:
- Diarrhea (loose stools) or more bowel movements than usual
- Blood in your stools or dark, tarry, sticky stools
- Severe stomach-area (abdomen) pain or tenderness.

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:
- Yellowing of your skin or the whites of your eyes
- Severe nausea or vomiting
- Pain on the right side of your stomach area (abdomen)
- Drowsiness
- Dark urine (tea colored)
- Bleeding or bruising more easily than normal
- Feeling less hungry than usual
- Decreased energy

Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:

- Headaches that will not go away or unusual headaches
- Extreme tiredness
- Weight gain or weight loss
- Dizziness or fainting
- Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
- Hair loss
- Feeling cold
- Constipation
- Voice gets deeper
- Excessive thirst or lots of urine.

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

- Decrease in the amount of urine
- Swelling in your ankles
- Blood in your urine
- Loss of appetite.

Skin Problems. Signs of these problems may include:

- Rash
- Skin blistering
- Itching
- Ulcers in mouth or other mucous membranes.

Inflammation of the brain (encephalitis). Signs and symptoms of encephalitis may include:

- Headache
- Fever
- Tiredness or weakness
- Confusion
- Memory problems
- Sleepiness
- Seeing or hearing things that are not really there (hallucinations)
- Seizures
- Stiff neck.

Problems in other organs. Signs of these problems may include:

- Changes in eyesight

- Severe muscle weakness
- Severe or persistent muscle or joint pains
- Chest pain

Getting medical treatment right away may keep these problems from becoming more serious. Your study doctor will check you for these problems during treatment with Opdivo. Your study doctor may treat you with corticosteroid or hormone replacement medicines. Your study doctor may also need to delay or completely stop treatment with OPDIVO, if you have severe side effects.

What should I tell my study doctor before receiving Opdivo? Before you receive Opdivo, tell your study doctor if you:

- Have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- Have had an organ transplant
- Have lung or breathing problems
- Have liver problems
- Have any other medical conditions
- Are pregnant or plan to become pregnant. It is unknown at this time if Opdivo is harmful to a fetus.
  - Females who are able to become pregnant should use an acceptable method of birth control during and for 23 weeks after your last dose of Opdivo (more about this below). Talk to your study doctor about birth control methods that you can use during this time.
  - Tell your study doctor right away if you become pregnant during treatment with Opdivo.
- Are breastfeeding or plan to breastfeed. It is not known if Opdivo passes into your breast milk. Do not breastfeed during treatment with Opdivo and for 23 weeks after your last dose.

Tell your study doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your study doctor and pharmacist when you get a new medicine.

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

Very common side effects of nivolumab are: [≥1/10 or ≥10%]

- Diarrhea
- Fatigue
- Itching
- Rash

Common side effects of nivolumab include: [≥ 1/100 to < 1/10 or ≥ 1% to <10%]

- Abdominal pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- Allergic reaction/hypersensitivity
- ALT increased: lab test result associated with abnormal liver function
- Amylase increased: lab test result associated with pancreas inflammation
- AST increased: lab test result associated with abnormal liver function
- Bilirubin (liver function blood test) increased
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased appetite
- Dizziness or vertigo (feeling off balance which can lead to dizziness)
- Dry mouth
- Dry skin
- Fever
- Headache
- High blood pressure
- Increased blood sugar
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Joint pain or stiffness
- Lipase increased: lab test result associated with pancreas inflammation
- Loss of color (pigment) from areas of skin
- Lung inflammation (pneumonitis - see details below)
- Musculoskeletal pain
- Nausea
- Redness (of the skin)
- Shortness of breath
- Sodium levels in the blood low
- Swelling, including face, arms, and legs
- Thyroid gland function decreased/thyroid stimulating hormone increased (lab test associated with abnormal thyroid function)
- Thyroid gland function increased
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Upper respiratory tract infection
- Vomiting

Uncommon side effects of nivolumab include: [≥ 1/1,000 to < 1/100 or ≥0.1% to <1%]

- Adrenal gland function decreased
- Bronchitis
- Cranial nerve disorder
- Diabetes
- Dry eye
- Hair loss
- Heart rate increase
- Heart rhythm abnormal
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Liver inflammation
- Low blood pressure
- Lung infiltrates, associated with infection or inflammation
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Renal (kidney) failure or kidney injury
- Respiratory failure
- Vision blurred

Rare side effects of nivolumab include: [≥ 1/10,000 to < 1/1,000 or ≥0.01% to <0.1%]

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

- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.
- Vogt Koyanagi Harada syndrome; a disease that affects the pigmented tissue; this may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss, ringing in the ears and /or the skin leading to loss of skin color

Lung Inflammation (pneumonitis): It is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported infrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest x-rays and/or CT scans.

Please inform your study doctor or nurse AT ONCE if you experience any of the following:

- Any new or increased shortness of breath
- Any new or increased chest pain
- Any new or increased pain/difficulty while breathing
- Any new or increased cough or any significant change in your type of cough; for example, any new or increased mucous or blood in your cough
- Any change in the amount of oxygen you require
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms

Reproductive Risks

Female patients:

Patients should not become pregnant while on this study because the study treatments in this study could affect an unborn baby. Breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to an unborn child/infant, you should not become pregnant or nurse a baby while on this study. Females able to have a child must have a negative pregnancy test prior to enrolling in the study. Female patients must meet 1 of the following conditions:

- Patient is postmenopausal – i.e. amenorrheic (no menstrual period) without alternative medical cause – for at least 1 year prior to the date of signed informed consent. Note: If menopausal status is considered for the purpose of evaluating childbearing potential, then postmenopausal status in females < 55 years of age will be confirmed with a blood test for follicle stimulating hormone (FSH level).
- Patient is surgically sterile (i.e. patient has had a bilateral oophorectomy, or a complete hysterectomy), or patient's partner is surgically sterile (i.e. has had a vasectomy), or
- If of childbearing potential, female patient agrees to practice 2 methods of acceptable contraception (with 1 method being highly effective and the other method being either highly effective or less effective, as listed in the below table) at the same time, from the time of signing the informed consent, and for 23 weeks after patient's last dose of vorolanib or nivolumab (whichever dose occurs last), or
- Patient agrees to practice true abstinence (defined as complete avoidance of heterosexual intercourse), when this is in line with the preferred and usual lifestyle of the patient.

Female patients of childbearing potential must use acceptable contraception from time of signing consent until 23 weeks after the last dose of study medication.

Male patients:

You should not father a child while on this study because the study treatments in this study could affect an unborn baby. Participation in this study may affect your ability to father a child. For future childbearing, you may wish to consider banking sperm prior to beginning this study. Due to unknown risks and potential harm to an unborn child/infant, you should not get a partner pregnant while you are getting the study treatment. Male patients must meet 1 of the following conditions:

- Patient is surgically sterile (has had a vasectomy), or patient's sexual partner is not a woman able to have children, or
- Patient agrees to practice 2 methods of acceptable contraception (with 1 method being highly effective and the other method being either highly effective or less effective, as listed in the below table) at the same time, from the time of signing the informed consent, and for 31 weeks after patient's last dose of VOROLANIB or nivolumab (whichever dose occurs last), or
- Patient agrees to practice true abstinence (defined as complete avoidance of heterosexual intercourse), when this is in line with the preferred and usual lifestyle of the patient.

Male patients who are not surgically sterile and who are sexually active with women of child bearing potential must use acceptable contraception from the time of signing consent until 31 weeks after the last dose of study

medication.

All patients (male or female):

- If your partner becomes pregnant during this study, you must tell the study doctor immediately. The study doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. For female patients who become pregnant while on this study, the study treatment will be stopped immediately and the pregnancy will be followed until conclusion. For partners of male patients who become pregnant, we will ask for permission to follow the pregnancy. We may al so request information on pregnancy outcomes and breast-feeding. Bristol-Meyers Squibb, the maker of nivolumab, will receive this information.

Methods of Contraception

HIGHLY EFFECTIVE methods of contraception:

- Male condoms with spermicide
- Hormonal methods of contraception including combined oral contraceptive pills, vaginal ring, injectables, implants and intrauterine devices (IUDs) such as Mirena®. Female partners of male patients participating in the study may use hormone based contraceptives as one of the acceptable methods of contraception since they will not be receiving study drug.
- Nonhormonal IUDs, such as ParaGard®.
- Tubal ligation.
- Vasectomy.
- Complete Abstinence*.
  - * Complete abstinence is defined as complete avoidance of heterosexual intercourse and is an acceptable form of contraception for all study drugs. Subjects who choose complete abstinence are not required to use a second method of contraception, but female subjects of childbearing potential must continue to have pregnancy tests. Acceptable alternate methods of highly effective contraception must be discussed in the event that the patient chooses to stop complete abstinence.

LESS EFFECTIVE methods of contraception:

- Diaphragm with spermicide.
- Cervical cap with spermicide.
- Vaginal sponge.
- Male Condom without spermicide.
- Progestin only pills by female patient able to have children, or by male patient's partner who is a female able to have children.

- Female Condom*.
  * A male and female condom must not be used together.

Other Risks

Allergic Reaction

It is possible to have an allergic reaction to the study treatment. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are: rash, having a hard time breathing, wheezing, a sudden drop in blood pressure (making you feel dizzy or lightheaded), swelling around the mouth, throat, or eyes, a fast pulse or sweating.

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

Computed Tomography Scans (CT Scans)

CT scans are used to create images of internal bones and organs using radiation.
The contrast solution that may be given for a CT scan may cause an allergic reaction (rare). Severe allergic reactions can be life threatening. CT contrast solution can cause kidney damage, especially if you are diabetic, dehydrated (lost body water) or elderly. CT contrast is used in scans to highlight specific parts of the body.

During CT scans, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel anxiety in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your doctor. Your doctor may give you a medication in an effort to make you feel more comfortable in a confined space.

Radiation Risks

Participation in this research study could involve exposure to radiation from two CT scans of your chest and abdomen, and possibly your pelvis and head (depending on where your cancer is located). This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you could receive by participating in this study is equal to your body receiving about 8 years of radiation from your natural surroundings or about 50% of the exposure allowed for radiation workers in one year.

Magnetic Resonance Imaging (MRI)

This is a medical imaging technique used to investigate the anatomy of the body and its risks include claustrophobia, discomfort due to lying still for a prolonged period of time, and other factors which will be described to you and discussed with you by the MRI staff.

Blood Draw Risks

When you give blood, you may feel faint, or experience mild pain, bruising, irritation or redness at the site. In rare cases, you may get an infection.

Risk of Loss of Confidentiality

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or employment discrimination based on genetic information.

The law provides that health insurance companies and group health plans
- may not ask for genetic information from this research and
- may not use genetic information when making decision about eligibility or premiums

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law also will not help you get other types of insurance (such as: life, disability or long-term care).

Despite the GINA protections and the best efforts of the research team, there may still be a risk if information about you were to become known to people outside of this study.

To minimize this risk, we will remove your name and any other information that could directly identify you from your materials. We will replace this information with codes. We will keep a master list that links those codes to your materials. Only certain project staff can access this master list. We will keep the samples in locked freezers in locked buildings. We will keep health information and research data on secure computers. These computers have many levels of protection.

Your name and other information that could directly identify you (such as address or social security number) will not be placed into any database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:

a) The benefits to science and humankind that might result from this study:

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This research may contribute to the understanding of cancer and its treatment, and may eventually lead to improvements in treatment.

b) The benefits you might get from being in this study:
There may or may not be a direct benefit to you as a result of your participation in the study.

Procedures to be followed:

Screening

The following must be completed ≤ 28 days prior to your first dose of study treatment:

- Scan of your disease by CT or MRI. Scanning to include at least your chest and abdomen, with any additional areas (such as the pelvis) as deemed appropriate by your study doctor. Also, if it is known or suspected by your study doctor that your disease has spread to your brain or spinal cord (CNS metastasis), you will have a scan of your head by CT or if preferable MRI.

- Blood sample (about $^1/_3$ tablespoon) will be tested for Hepatitis B and Hepatitis C (infectious diseases primarily involving the liver, which are caused by the hepatitis B and C viruses). Patients with Hepatitis B or uncontrolled Hepatitis C are not eligible to receive the study treatment.
    - Please note that if test results show that you are positive for Hepatitis B or C, the study staff will tell you the results. We would talk with you before and after testing, and these test results will be given to you only in person. You should know that the study staff must give your name to the Tennessee Department of Health if you test positive for Hepatitis B or C because this is the law. If others find out you have one or more of these viruses, it may cause mental stress, unfair treatment from other people, problems with being able to get insurance or find a job, or other unknown problems. It is important to seek medical care if you have these diseases.

Your study team will request a sample of your tumor tissue. The purpose of this important tissue is to help understand why different patients do or do not respond to the study treatment.

- Your demographics (for example, age, race and gender) will be reviewed. You will be asked about your past and current health, including any past treatments for your condition.
- You will have a physical exam. Your weight and vital signs will be recorded (blood pressure, heart rate and temperature).
- Oxygen saturation: The oxygen level in your blood will be measured by pulse oximetry. (A small non-invasive device similar to a clothespin will gently squeeze a body part, for example finger or earlobe, in order to measure the oxygen saturation in your blood.)
- Your health will be assessed by questions about your ability to carry out daily activities.

- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Urine test (about ¼ cup of urine will be collected) to check your kidney function.
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell).
  - Check your Chemistries (proteins, elements and minerals in your blood).
  - Check your Thyroid function (hormone levels in the blood).
  - Women Only: During screening, a blood pregnancy test will be done during for women who can have children (about ⅓ tablespoon of blood will be drawn). This pregnancy test must be negative for you to take part in the study. Women who are pregnant or breast feeding may not take part in the study. If you are a post-menopausal woman (a woman who can no longer become pregnant), a portion of the above blood collected for blood chemistries may be used to also measure follicle stimulating hormone (FSH) to confirm your post-menopausal status.
- 12-Lead Electrocardiogram (ECG) to check the electrical activity of your heart, using 12 sticky pads attached to the surface of your skin.

Treatment

If, based on the results of the above screening tests and procedures, you qualify and choose to participa te in the study, you will return to your study doctor's office to begin treatment.

Cycle 1, Day 1

- Your health will be assessed by questions about your ability to carry out daily activities.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Blood will be drawn (about 2 tablespoon) for the following:
  - Blood sample for research to look for possible differences in genes (also known as DNA) that may influence how different patients do or do not respond to the study treatment.
  - Blood samples to study biomarkers for research. (Biomarkers are biological indicators of how your body and illness may be reacting to the drugs that you are receiving.)
- You will start taking oral vorolanib by mouth (once per day).
- You will receive your first dose of nivolumab by a 30 minute infusion into a vein.

The following will be done, unless already completed ≤ 7 days prior to your first dose of vorolanib/nivolumab:

- Physical exam.
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)

- Check your Chemistries (proteins, elements and minerals in your blood)
- Urine test (about ¼ cup of urine will be collected) to check your kidney function.

Cycle 1, Day 8 (Only if you are in the dose escalation part of this study will you have this visit)

- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood)

Cycle 1, Day 15

- Physical exam.
- Your health will be assessed by questions about your ability to carry out daily activities.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood)

- Nivolumab infusion by a 30 minute infusion into a vein.

Cycle 1, Day 22 (Only if you are in the dose escalation part of this study will you have this visit)

- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood).

Cycle 1, Day 29

- Physical exam.
- Your health will be assessed by questions about your ability to carry out daily activities.

- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood).
  - Check your Thyroid function (hormone levels in the blood).
- Blood will be drawn (about 2 tablespoon) for the following:
  - Blood sample for research to look for possible differences in genes (also known as DNA) that may influence how different patients do or do not respond to the study treatment.
  - Blood samples to study biomarkers for research. (Biomarkers are biological indicators of how your body and illness may be reacting to the drugs that you are receiving.)
- Urine test (about ¼ cup of urine will be collected) to check your kidney function.
- Nivolumab infusion by a 30 minute infusion into a vein.

<u>Cycle 1, Day 43</u>

- Physical exam.
- Your health will be assessed by questions about your ability to carry out daily activities.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- Blood will be drawn (about ½ tablespoon) to check the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood)
- Nivolumab infusion by a 30 minutes infusion into a vein.

<u>Cycle 1, between Days 50-56</u>:

- Standard of Care re-scanning of your disease by CT or MRI to occur during Week 8 (ideally on Day 56), prior to initiating Cycle 2 treatment. Scanning to include at least your chest and abdomen, with additional sites of known or suspected disease (for example, pelvis) as clinically indicated according to your study doctor. Additional scans or increased scan frequency may be performed according to the medical judgment of your study doctor.
- Also, if a baseline scan done during screening previously showed that your disease had spread to your brain or spinal cord (CNS metastasis), standard of care re-scanning of your head by CT or by preferable MRI will be done at least every 3 months since your prior head scan.

<u>Additional Cycles, Day 1</u>

In general, you may continue to receive treatment on this study as long as you tolerate treatment and your disease does not get worse (progress). All additional cycles will continue as outlined above with the exception that we will no longer collect blood samples for genetics (Pharmacogenetics) and biomarkers (Pharmacodynamics)

Cycle 2+:
After the first 16 weeks (2 cycles), if you have not experienced disease progression (non-PD response), patients with continued clinical benefit can switch to treatment with 480 mg nivolumab every 4 weeks on Days 1 and 29 of each 56-day cycle.

End-of-Treatment and Follow-up

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

End-of-Treatment / Withdrawal Assessments
The following must be completed subsequent to and not later than 14 days after you permanently discontinue study treatment with vorolanib/ nivolumab (whichever treatment occurs last) and prior to any subsequent anti-cancer therapy:

- Physical Exam.
- Your health (ability to carry out your daily activities) will be assessed.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- 12-Lead Electrocardiogram (ECG) to check the electrical activity of your heart, using 12 sticky pads attached to the surface of your skin.
- Urine test (about ¼ cup of urine will be collected) to check your kidney function.
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood)
  - Check your Thyroid function (hormone levels in the blood)
- Blood will be drawn (about 2 tablespoon) for the following:
  - Blood sample for research to look for possible differences in genes (also known as DNA) that may influence how different patients do or do not respond to the study treatment.
  - Blood samples to study biomarkers for research. (Biomarkers are biological indicators of how your body and illness may be reacting to the drugs that you are receiving.)
- If prior scans done > 28 days before: Re-scanning of your disease by CT or MRI. This scan would be done for research purposes. Scanning to include at least your chest and abdomen, with additional

sites of known or suspected disease (for example, pelvis) as clinically indicated according to your study doctor. Additional scans may be performed according to the medical judgment of your study doctor (including possible head imaging, if medically appropriate to repeat). Also, if you stop the study for reason other than progressive disease confirmed by CT or MRI (for example, stopping the study treatment because of side effects), then CT or MRI scans involving sites of known or suspected disease must be continued every 8 weeks (± 7 days) until disease progression is confirmed by imaging. These scans will be done as part of your standard care.

28-Day Follow-Up Visit Assessments

You will be asked to return to the study clinic 28 days after your final treatment with VOROLANIB or nivolumab (whichever occurs last), in order to undergo the following:

- Physical Exam.
- Your health (ability to carry out your daily activities) will be assessed.
- Your weight, vital signs (blood pressure, heart rate and temperature), and oxygen saturation will be recorded.
- You will be asked about any problems you are having and the medicines you are taking, including all prescriptions and over-the-counter medicines.
- 12-Lead Electrocardiogram (ECG) to check the electrical activity of your heart, using 12 sticky pads attached to the surface of your skin.
- Urine test (about ¼ cup of urine will be collected) to check your kidney function.
- Blood will be drawn (about ½ tablespoon) for the following:
  - Check your Blood Cell Counts (numbers of each type of blood cell)
  - Check your Chemistries (proteins, elements and minerals in your blood)
  - Check your thyroid function (hormone levels in the blood).

100-Day Follow-Up Visit Assessment

100 days after your final treatment with vorolanib or nivolumab (whichever occurs last), you will be contacted either by a clinic visit, or by a telephone call from a member of your study team. If you are having any possible side effects after stopping the study treatment, you may be asked to have more tests done to check your heath (such as repeating some or all of the above items previously done during your 28-Day follow-up assessment).

Long-Term Follow-Up

After you complete all of the planned study visits, you will be contacted approximately every 3 months (± 14 days) after your final treatment with vorolanib or nivolumab (whichever occurs last), in order to determine your health status. Contact could be by a variety of methods, including via telephone, clinic visit, medical records, or publicly available information. This will continue until death, end of the study, until you withdraw consent for this communication, or for a maximum of 2 years after your final treatment with vorolanib/ nivolumab –whichever comes first.

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Leftover Specimens

Any leftover study tissue or blood samples may be stored for future research studies. Any studies that use these leftover samples will be approved by an Institutional Review Board.

Your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

Payments for your time spent taking part in this study or expenses:

You will not be paid for participating in this study.

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

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There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Katy Beckermann, PhD, MD at (615) 936-8422. If you cannot reach the research staff, please page the study doctor at (615) 322-5000.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:

The study doctor, sponsor, supporters Bristol-Myers Squibb or Equinox/ Xcovery, or a regulatory authority (FDA, Institutional Review Board, etc.) may choose to end your participation in this study without your consent. This could happen for reasons such as:

- The study doctor feels it is not in your best interest to continue in the study
- You fail to follow the study doctor's instructions
- You experience an adverse reaction that requires other medical treatment
- You become pregnant, or
- The sponsor, supporters: Equinox/ Xcovery or Bristol-Myers Squibb, or the FDA or other regulatory authority stops the study for any reason.

If you are removed from the study, the reason will be explained to you.

What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

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Clinical Trials Registry:

A description of this clinical trial will be available on 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.

Clinical Trials Reporting Program:
Vanderbilt's NCI-Designated Cancer Center or the Sponsor registers National Cancer Institute (NCI)-supported clinical trials with NCI though their Clinical Trials Reporting Program (CTRP) to provide study related information. The data provided will include the following identifiable information that may identify you: birth month/year and five-digit zip code. NCI uses the data to manage and enhance the nation's investment in cancer research.

Confidentiality:

All efforts, within reason, will be made to keep your personal information in your research record confidential but total confidentiality cannot be guaranteed. Your information and samples will be given a unique code instead of your name to help protect your identity. Dr. Beckermann, her staff at Vanderbilt and other authorized people will be the only people who know your personal information. Results of this study may be presented in meetings or in publications. Your identity will not be released in those presentations. Your study records will be secured in the clinical trials office. Your research data will be kept for an unknown period of time. Your tissue and blood samples will be kept in locked storage and may be used or stored indefinitely from the end of the study. Any samples that are not needed will be destroyed.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Beckermann and her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

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Privacy:

Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you.

Study results:
You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Beckermann and her study team may share the results of your study and/or non-study linked blood and other tissue samples and related records, medical histories, physical examinations, laboratory tests, x-rays, CT/MRI scans, ECG results, and any other data created or collected during the study, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Medical Center Institutional Review Board, domestic and foreign drug regulatory agencies such as the Food and Drug Administration, National Institutes of Health, National Cancer Institute, representatives of Equinox/Xcovery, Bristol-Myers Squibb, Scientific Review Committees, Medicare and Insurance companies for billing purposes, etc. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Beckermann in writing and let her know that you withdraw your consent. Her mailing address is: Katy Beckerman, PhD, MD, Vanderbilt-Ingram Cancer Center, 777 Preston Research Building, 2220 Pierce Avenue, Nashville, TN 37232. At

that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title