Title of Study: A Phase 2 Multi-Center Pharmacodynamic Study of TVB-2640 in KRAS Mutant Non-Small Cell Lung Carcinomas

Consent and Authorization to be part of a Research Study
To be conducted at

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
University of Cincinnati

Key Information about this Study

This is a research study to find out whether an investigational (non-FDA approved) drug called TVB-2640 can treat advanced KRAS mutant lung cancer better or more safely than standard medication. The word "investigational' means the TVB-2640 is still being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA).

To begin the study, you will sign this informed consent form and begin a screening period of up to 28 days to see if you are eligible for this study. During screening, we will review your medical history, demographics, past and current medications, perform a full physical exam (including vital signs, height, and weight), have you answer study questionnaires about your health and how you are feeling, eye exam, draw your blood, collect urine, have imaging of your neck, chest, abdomen, and/or pelvis (depending on known areas of cancer), perform a 12-lead electrocardiogram (EKG), perform a echocardiogram (ECHO). We also may offer a nutritional consultation to discuss any food recommendations and strategies for managing potential nausea, diarrhea, and appetite changes experienced with the study drug. If available, we will collect some existing (archival) tumor tissue. It may be necessary for you to come to the clinic several times a week during the screening period.

If you are eligible and agree to join the study, you will begin study treatment. In this study, patients will receive the standard approved daily dose of TVB-2640 (100 mg/m2). Patients will take TVB-2640 orally (by mouth) once a day for 4 week cycles. A Cycle is a length of time you are taking a drug for. TVB-2640 should be taken with a glass of water about the same time each day without food (at least one hour before or at least two hours after a meal). Patients should not cut or chew the tablets. Patients may continue study treatment until their disease worsens (progression), another illness preventing further study treatment, unacceptable side effects, you decide to withdraw from the study or the study doctor(s) decides further study treatment is unacceptable for you.

The most common side effects you may experience from TVB-2640 include fatigue, hair loss, dry skin, decreased appetite, redness, swelling, and pain on the palms of hands and/or soles of the feet called Hand-foot syndrome. You will be monitored closely for any side effects. Additional side effects or risks related to your participation in this study are included later in this consent form.

Some procedures and tests for this study will be provided free of charge. However, you or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as physical exams, CT or MRI scans, routine safety blood tests, any medications given or prescribed to help or prevent side effects and optional tumor tissue collection.

If you participate in this study, you will be on treatment until your disease gets worse (you may continue for longer if it is determined you are still benefitting from the study treatment).

Title of Study: A Phase 2 Multi-Center Pharmacodynamic Study of TVB-2640 in KRAS Mutant Non-Small Cell Lung Carcinomas

Information about this form

You may be eligible to take part in a research study. This is a multi-site study, meaning it will take place at several locations. Because this is a multi-site study the informed consent form will includes two parts. This form is Part 1 and includes information that applies to all study sites, like the purpose of the study and the research procedures to be conducted.

Part 2 of the consent form will include information specific to the study site where you are being asked to enroll. This could include any research procedures specific to a study site or local contact information for the study team.
Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the staff or doctors at your local institution. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the local institution, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is David Gerber, MD,, Department of Hematology/Oncology at the University of Texas Southwestern Medical Center.

Funding
The Gateway Foundation, a non-profit organization that promotes scientific research, is funding this study. This organization is providing money to the University of Texas Southwestern Medical Center so that the researchers can conduct the study.

Purpose – "Why is this study being done?"

You are asked to participate in this research study of non-small cell lung cancer that may have a mutation (defect) in the KRAS gene in the tumor.

The researchers hope to learn whether an investigational (non-FDA approved) drug called TVB-2640 can treat advanced KRAS mutant lung cancer better or more safely than standard medication. The word "investigational" means the TVB-2640 is still being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA).

Additionally, this study is being done to determine whether [11C] Acetate PET/CT scans can help predict therapy response in patients with KRAS mutant lung cancer. A PET (positron emission scan) is a scan to help show how organs and tissues are working. Tumor metabolism is a series of reactions tumors use as they burn sugar or acetate or other metabolites for fuel. [11C]Acetate is an experimental radioactive material, which moves through your body after it has been injected into one of your veins. The PET/CT scan will be able to trace the small amount of [11C]Acetate and reveal areas in your body that are using [11C]Acetate for fuel. Regulatory bodies that oversee the use of drugs and radiotracers in the US have not approved the sale or use of [11C]Acetate, although it is used in approved research studies in the US and clinical studies in other countries. The [11C] Acetate PET/CT scans will only be performed at UT Southwestern.

Investigational Use of Drug or Device
This study involves the use of an investigational drug called TVB-2640. "Investigational" means that the drug has not yet been approved by the U.S. Food & Drug Administration (FDA) for treating advanced KRAS mutant lung cancer better or more safely than standard medication.

This study will help find out what effects, good and/or bad, this drug has on people who take it and on its effect on the advanced KRAS mutant lung cancer..

The study drug used in this study has not been given to people before, so it is not known what side effects may occur but, from other testing that has been done, it may cause none, some, or all of the side effects listed below. There may also be other side effects that the sponsor or your doctor cannot predict. You should discuss any concerns with your study doctor.

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.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you have non-small cell lung cancer that may have a mutation (defect) in the KRAS gene in the tumor.

How many people are expected to take part in this study?
This study will enroll approximately 34 study participants across all study sites.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, the number of visits you will have with the researchers or study staff will depend on how long you receive treatment on this trial.

It may be necessary for you to return to the hospital/clinic every twice during the first month of treatment then every 4 weeks while you are receiving the study medication. Follow-up visits will occur every 4 weeks until you start another type of cancer treatment or your cancer worsens. If you are experiencing any severe side effects, you may be asked to come in for a visit past 8 weeks, until the side effects have gone away. These follow-up visits will take approximately 2-3 hours, depending on if you have scans on the same day of the visit.

The total length of time that you will be on the study depends on if and for how long, you respond to the

treatment. You may continue to receive TVB-2640 daily for as long as your doctor feels that you are benefiting from the study drug, or until you have side effects that you cannot tolerate. You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. Many of the procedures are described below as "**standard care**" and would be done even if you do not take part in this research study. You will be told which ones are for "**research only**".

Screening Procedures

To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- We will confirm that you have KRAS mutant Lung Cancer. This is done by testing the tissue that was collected during a previous biopsy. If tissue is not available for testing, this test may be done using blood. **(Standard Care)**
- Your medical history and demographic data (this includes information about your gender, age, and race/ethnicity) will be recorded. **(Standard Care)**
- You will be asked about any medications you are currently taking. **(Standard Care)**
- A Physical examination will be done which will include body weight, height, and vital signs (heart rate, blood pressure, temperature) **(Standard Care)**
- A performance assessment (evaluation of your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale. **(Standard Care)**
- A urine sample will be taken for routine tests. **(Standard Care)**
- Blood samples (30 mL; about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), how well your organs are functioning including your thyroid, kidneys and/or liver and to check for hepatitis (a liver disease) **(Some tests will be Standard and some will be Research)**
- An electrocardiogram (EKG) which records the electrical activity of your heart will be performed **(Research)**
- An echocardiogram (ECHO) which is a 3D image of your heart will be completed. **(Research)**
- If you are a woman who is able to become pregnant, a blood or urine sample will be collected to test if you are pregnant. **(Standard Care)**
- You will have an Eye Exam **(Research)**
- You will have blood collected (10mL; about 2 teaspoons) for plasma lipidomics. This test looks to see if the study drug changed the fat particles in your blood to help stop the growth of the cancer. For this blood test, we will ask you to fast for 12 hours prior to the lab appointment. This sample may be drawn on Cycle 1 Day 1. **(Research)**
- You will have blood collection (6ml; about 1 teaspoon) for pharmacokinetics (PK) to look at how fast the drug is absorbed in the body. This sample may be drawn on Cycle 1 Day 1. **(Research)**
- A measurement of your tumor will be done by computed tomography scan (CT scan) or a magnetic

resonance scan (MRI) of your chest and abdomen if you haven't had one in the last 28 days. **(Standard Care)**

- If your doctor normally monitors you for brain metastases, an MRI of your brain will be performed. If you cannot have an MRI, we may do a CT scan of your head. **(Standard Care)**
- ^{11}C-acetate PET Scan (performed only at UTSW site). You will sign a separate consent form for this procedure. This is a whole body scan. For this scan you will be asked to lie down on your back. An intravenous (IV) catheter (tube) will be placed in a vein in your arm. This IV will be used to infuse the ^{11}C-acetate. ^{11}C-acetate is a radioactive liquid used to measure the tumor's metabolic rate or metabolism. The scan will take approximately 90 minutes. You will be contacted by phone the following day to ensure you are doing fine. This call will last 5-10 minutes. **(Research)**

  The [11C]Acetate PET imaging test is designed for research, not for medical purposes. Even though the researchers are looking at your imaging tests, the [11C]Acetate PET/CT scan analysis will not be used for medical purposes; the result will not be sent to you or your regular doctor. However, if during [11C]Acetate PET CT scan imaging, something unusual and important finding is noticed then you and your treating doctor will be notified immediately.
- Quality of Life Assessment. Questionnaires will be completed at baseline, at each disease assessment (every 2 treatment cycles or 8 weeks), and at end-of-treatment. **(Research)**
- We will collect some existing (archival) tumor tissue from a previous biopsy, if available.

This visit will take approximately 3-5 hours, depending on if you have all procedures done during the same visit on the same day. Research procedures will add approximately 2-3 hours to the length of a routine care visit.

The screening procedures will be completed over several visits. Multiple procedures are performed through different departments, so scheduling will be based on appointment availability. The study team will try to schedule multiple visits within the same day to reduce the number of times you have to return to clinic during screening.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you.

Study Procedures - as a participant, you will undergo the following procedures:

Cycle 1 Day of Treatment with TVB-2640

- You will have a physical examination including body weight, height, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (30mL; about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- A member of the study team will cleans your forehead skin and apply 4 small sticker-like patches on your forehead. The patches will be placed in your forehead in clinic prior to taking the TVB-2640. You will be asked to leave the patches on for about 30 minutes. The patches will then be removed and stored for testing. These patches are used to measure the amount of sebum (oil) on your skin.
- You will meet with a pharmacist to answer any questions about taking TVB-2640.

This visit will take approximately 2-3 hours.

Cycle 1 Day 8

- You will be asked to return to clinic for blood collection (6ml; about 1 teaspoon per timepoint) at 3 time points on this day. These blood draws are for pharmacokinetics (PK) to look at how fast the drug is absorbed in the body. You will be asked to take your medication at a certain time the day before this visit and to hold you medication until you are in clinic. You will take this day's dose in clinic with the study coordinator.

You will be assigned to have blood collected at certain time points this day based on when you join the study. The time points will be as follows, depending on which group you are assigned to:

Cycle 1 Day 8 PK TIME POINTS	Group 1	Group 2	Group 3	Group 4
Sampling Time point				
Cycle 1, Day 8: 24 hours after you took the TVB2640 on Cycle 1 Day 7	X	X	X	X
Cycle 1, Day 8: 30 minutes after you take the TVB2640 in clinic	X			
Cycle 1, Day 8: 4 hours after you take the TVB2640 in clinic	X			
Cycle 1, Day 8: 1 Hour after you take the TVB2640 in clinic		X		
Cycle 1, Day 8: 5 Hours after you take the TVB2640 in clinic		X		
Cycle 1, Day 8: 2 Hours after you take the TVB2640 in clinic			X	
Cycle 1, Day 8: 6 Hours after you take the TVB2640 in clinic			X	
Cycle 1, Day 8: 3 Hours after you take the TVB2640 in clinic				X
Cycle 1, Day 8: 8 Hours after you take the TVB2640 in clinic				X

In total, you will have about 3 teaspoons of blood collected on this day.

Cycle 2 Day 1 of Treatment with TVB-2640:

- You will have a physical examination including body weight, height, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (30mL; about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will have blood collected (10mL; about 2 teaspoons) for plasma lipidomics. This test looks to see if the study drug changed the fat particles in your blood to help stop the growth of the cancer. For this blood test, we will ask you to fast for 12 hours prior to the lab appointment.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
  - A member of the study team will clean your forehead skin and apply 4 small sticker-like patches on your forehead. The patches will be placed in your forehead in clinic prior to taking the TVB-2640. You will be asked to leave the patches on for about 30 minutes. The patches will then be removed and stored for testing. These patches are used to measure the amount of sebum (oil) on your skin.
- ^{11}C-acetate PET Scan. This is a whole body scan done for research. For this scan you will be asked to lie down on your back. An intravenous catheter (IVs) will be placed in a vein of your arm. This IV will be used to infuse the ^{11}C-acetate. ^{11}C-acetate is a radioactive liquid used to measure the tumor's metabolic rate or metabolism. The scan will take approximately 90minutes.

  This visit will take approximately 4-6 hours. The 11C-acetate PET Scan may be completed within 3 days surrounding this visit.

Cycle and Beyond Day 1 of Treatment with TVB-2640:

- You will have a physical examination including body weight, height, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (30mL; about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- During your visit, an electrocardiogram (EKG) which records the electrical activity of your heart will be performed.
- At every other cycle, you will be asked to fill out 2 quality of life questionnaires

This visit will take approximately 2-3 hours.

Every 8 weeks while taking TVB-2640:

You will have a CT or MRI scan of your chest and abdomen to see how your disease is responding to treatment. Quality of Life Assessment Questionnaires will be completed at baseline, at each disease assessment (every 2 treatment cycles or 8 weeks), and at end-of-treatment.

End of Treatment and Follow Up

When you stop taking TVB-2640 you will be asked to come in for an End of treatment and follow up visits. The follow up visits will occur every 4 weeks until you start another cancer treatment or your cancer worsens. If you are experiencing any severe side effects, you may be asked to come in for a visit past 8 weeks, until the side effects have gone away.

At these visits:

- You will have a physical examination including body weight, height, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (30mL; about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- During your visit, an electrocardiogram (EKG) which records the electrical activity of your heart will be performed.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- A measurement of your tumor will be done by computed tomography scan (CT scan) or a magnetic resonance scan (MRI) of your chest and abdomen (End of Treatment Only)

- Quality of Life Assessment. Questionnaires will be completed at baseline, at each disease assessment (every 2 treatment cycles or 8 weeks), and at end-of-treatment.

These visits will take approximately 2-3 hours, depending on if you have scans on the same day of the visit.

MRI

You will have an MRI of your chest and abdomen. For this procedure, you will lie still inside a large, doughnut-shaped magnet, also called the MRI scanner. The MRI technologist can see and hear you during the procedure. You will also be given a squeeze ball to use for communication. You will be inside the MRI scanner for approximately 45 minutes.

For the MRI procedure, you will receive a contrast agent. The contrast is used to highlight organs or tissues during imaging. For administration of the contrast, an intravenous catheter will be placed in your arm or hand. You will also have a blood test to measure your kidney function. For this test, approximately one teaspoon of blood will be drawn from your arm or hand.

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

The researchers will discuss your options for medical care when your participation in this study ends.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Risks – "What are the risks of participation in the research?"

Risks from the research

The investigators have designed this study to learn how well the new treatment(s) compare to commonly accepted treatment(s). There is a risk that the effectiveness and/or safety of the treatment for the study group may not be as good as the most commonly accepted treatments. You may get a treatment or drug that does

not help treat your disease or that makes your condition or disease worse.

Risks from the specific research procedures (drug(s), interventions, or procedures)
There are risks to taking part in this research study. One risk is that you may have side effects while on the study.

Side effects from this study will usually go away soon after you stop taking the TVB-2640.. In some cases, side effects can be long lasting or may never go away.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to each your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

Risks and side effects related to TVB-2640 include those which are:

TVB-2640

Cancer treatments often have side effects. The study drug used in this study has been given to 127 subjects so far. In 72 patients, it was given by itself, and in 55 subjects it was given in combination with another anticancer treatment called paclitaxel (Taxol). There may also be other side effects that the sponsor or your doctor cannot predict. You should discuss any concerns with your study doctor. Your study doctor may order other medications to make side effects less serious or to make you feel more comfortable (for example, anti-nausea drugs or antibiotics to treat infections).

<u>Frequent side Effects (occurring in over 20% of patients who have received TVB-2640):</u>

- Fatigue
- Hair loss
- Dry Skin
- Decreased appetite
- Redness, swelling, and pain on the palms of hands and/or soles of the feet called Hand-foot syndrome.

<u>Occasional side Effects (occurring in 2- 20% of patients who have received TVB-2640):</u>

- Eye problems such as inflammation and puffiness of eye and eyelids. Pain, itching, redness, dry eye(s), discharge, blurry vision, increase in tear production, reduced vision and or increased sensitivity to light from your eye(s). Your eyes will be examined by an eye doctor before you start taking TVB-2640. Your eyes must be considered healthy by the eye doctor before you are able to take part in the study. If you normally wear contact lenses, you must agree to refrain from wearing them during the time you are taking TVB-2640. If you have a condition known as "dry eye", and your doctor deems it moderate to severe, you will not be able to participate in this study.

- Gastrointestinal problems including nausea, vomiting, abdominal pain, diarrhea, constipation, decrease in appetite, dry mouth, dry lip, and/or inflammation of the mouth and lips (stomatitis) and/or gastrointestinal tract.
- Cough
- Dehydration (loss of water)
- Fever
- Shortness of breath
- Skin problems including dryness, redness, pain, itching, rash, sunlight sensitivity, thickening, inflammation, ulceration (formation of sores), scabs, and/or peeling may occur.
- Fluid retention (holding in) and swelling in the lower limbs
- Anemia (a condition of having a lower-than-normal number of red blood cells or quantity of hemoglobin)
- Salty or metallic taste in mouth
- Urinary tract infection
- Increase blood level of fatty acids called hypertriglyceridemia
- Weakness, numbness and/or pain or tingling in the hands or feet (may be without skin changes) called Peripheral Neuropathy
- Uncontrollable urge to move your legs called Restless Legs Syndrome
- Inflammation of the oral and/or gastrointestinal tract
- Changes to the respiratory system including inflammation of the lungs (pneumonitis). You will be asked at each visit to report any shortness of breath, and if you are concerned about these changes in between visits, you may contact your doctor by telephone to report these symptoms. Your doctor may ask that you come back for an unscheduled clinic visit.

In nonclinical studies using much higher doses than expected to be used in this study, the following observations were made:

- A slight prolongation of the QT interval (a measurement of the electrical activity in the heart) occurred, but went away after the study drug was stopped. A prolonged QTc interval can lead to irregular heartbeats (known as arrhythmia) and some types of arrhythmia can have serious consequences including death. This has not been seen to date in any of the patients treated with TVB-2640 alone or in combination with another type of therapy called a Taxol.

You will be asked at each visit to report any changes that you notice, and if you are concerned about these changes, you may contact your doctor by telephone in between clinic visits to report these changes. Your doctor may ask that you come back for an unscheduled clinic visit.

TVB-2640 is known as a type of drug called a small-molecule fatty acid synthase inhibitor (it prevents a chemical in your body known as fatty acid synthase from working properly). Drugs similar to TVB-2640 have been known to cause anorexia (loss of appetite for food) and weight loss.

- **If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.**

Magnetic Resonance Imaging (MRI):
An MRI is a way of looking at the soft tissues of the body. You will lie down on a large magnet. A magnetic signal will be sent through your body and then received back.

There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety (fear/worry) due to the loud, banging noise made by the machine while it is taking pictures and from staying in

a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time.

You may also experience some discomfort and fatigue from lying still during imaging.
If you have any metal clips or plates in your body, you should tell the investigator. MRI may not be appropriate if you are pregnant or are trying to become pregnant.

MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

• heart pacemaker, heart valve replacement, or aortic clips
• metal fragments in your eyes, skin, or elsewhere in your body
• brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
• venous umbrella
• pieces of metal in the body resulting from work as a sheet-metal worker or welder
• clips placed in an internal organ
• prosthetic devices, such as middle ear, eye, joint, or penile implants
• joint replacement.
• hearing aid that cannot be removed
• neurostimulator
• insulin pump
• intrauterine device (IUD)
• shunts or stents
• metal mesh or coil implants
• metal plate, pin, screws, or wires, or any other metal implants

Risks of Gadolinium (MRI Procedure):
The contrast agent you will receive is FDA-approved and used routinely for MRI exams. It contains a material called Gadolinium (dye used to highlight organs or tissues during imaging). The injection of Gadolinium may cause discomfort like headache, nausea, strange taste, or coldness at site of injection. These symptoms occur in less than 1 out of 20 patients receiving Gadolinium and go away quickly. There is a small risk of a severe allergic reaction that can cause breathing difficulties and/or low blood pressure; these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician and nursing staff will be available to evaluate and, if necessary, provide treatment. People with severe kidney failure who receive Gadolinium (dye used to highlight organs or tissues during imaging) are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF). This disease can cause widespread tissue scarring or hardening (fibrosis). In rare cases NSF can lead to lung and heart problems and cause death. If you have severe kidney failure and receive gadolinium, the risk of developing NSF is 1-5%. We may perform a blood test 30 days before your MRI to check how well your kidneys are working before you receive the Gadolinium. This test may be repeated closer to your MRI appointment if your medical condition has changed. If your kidneys are working at levels known to be at risk for NSF, you will not receive Gadolinium. You will not receive Gadolinium for research purposes if you have sickle cell disease (a disease of the blood cells) since it may put you at risk of developing hemolysis (breakdown of blood cells).

CT Scan:
A CT scan is a computerized series of detailed pictures of areas inside the body taken from different angles. You may feel some discomfort or anxiety when lying inside of the CT scanner. The dye that is injected into your body may cause you to get a metallic taste in your mouth, to feel warm, and rarely cause nausea and vomiting.

Risks of Radiation – Diagnostic Test
The radiation dose that you will get from diagnostic tests is medically indicated for your condition and it is the same that you would get if you were not involved in this research study.

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

You will have about 4 extra tablespoons of blood collected because you are in this research study.

Other Risks
There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

For more information about risks and side effects, ask one of the researchers or study staff.

There may be unforeseeable side effects that could be life threatening or fatal (could cause death).

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study early, please discuss your decision with the principal investigator. You will need to have the following procedures to safely withdraw:

- Return to the research center for tests that may be needed for your safety
- Return any unused study materials, including empty containers
- Discuss your future medical care, if any, with the researchers and/or your personal doctor

Reproductive Risks

Concerns for sexually active men and women: Women should not become pregnant and men should not father a baby while taking part in this study because we do not know how the study drugs/procedures could affect a man's sperm (for some drugs/procedures, the concern may be that the sperm might be affected and in some cases, drugs could being carried by the semen into the vagina and cause harm) or a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant or if you believe your female partner has become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed.

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the drug might affect a developing fetus. We will do a blood pregnancy test before you start treatment to make sure you are not pregnant.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs/procedures might have on their breast milk.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time, may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

Benefits – "How could you or others benefit from your taking part in this study?"

You may not receive any personal benefits from being in this study.

We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

There are other options available to you. Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Contact Information – Who can you contact if you have questions, concerns, comments, or complaints?

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at 214-648-3060.

This form is yours to keep.