THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase 1 Trial of Vandetanib (a multi-kinase inhibitor of EGFR, VEGFR and RET inhibitor) in Combination with Everolimus (an mTOR inhibitor) in Advanced Cancer
2011-0953

Subtitle: 0953

Study Chair: Sarina Piha-Paul

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to find the highest tolerable dose of the combination of vandetanib and everolimus that can be given to patients with advanced cancer. The effects of the study drugs at different dose levels and the safety of the study drugs will also be studied.

Vandetanib and everolimus are both designed to harm cancer cells, stopping their growth. This may stop or slow the growth or spread of cancer cells.

This is an investigational study. Vandetanib is FDA-approved and commercially available for the treatment of medullary thyroid carcinoma. Everolimus is FDA-approved and commercially available for the treatment of pancreatic neuroendocrine tumor, subependymal giant cell astrocytoma, and renal cell carcinoma. The use of these drugs in combination for the treatment of advanced cancer is investigational.

Taking the study drugs may help to control the disease. Future patients may benefit from what is learned in this study. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal. You may choose not to take part in this study because of potential costs and/or a prolonged stay out of town.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may continue taking the study drugs for as long as the study doctor thinks it is in your best interest.

You and/or your insurance provider will be responsible for the costs of vandetanib and everolimus during this study.

Your doctor will discuss standard treatment options with you, including their risks and benefits. You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. You will have screening tests to help the doctor decide if you are eligible to take part in this study. The following tests and procedures will be performed within 2 to 4 weeks before you may start receiving the study drugs:

- Your medical history will be recorded.
- You will have a physical exam, including measurement of your height, weight, and vital signs (blood pressure, heart rate, and temperature).
- You will be asked how well you are able to perform the normal activities of daily living (performance status).
- You will be asked about any drugs you may be taking and if you had any side effects from them.
- You will have an electrocardiogram (ECG) and an echocardiogram (ECHO) to check your heart function. If you have had an ECHO in the last 15 days, this test may not need to be repeated.
- Blood (about 2 teaspoons) and urine will be collected for routine tests.
- You will have an x-ray, computed tomography (CT) scan, positron emission tomography (PET) scan, and/or a magnetic resonance imaging (MRI) scan to check the status of the disease. If you have had one of these scans in the last 28 days, you may not need to have this repeated.
- If you have melanoma and the doctor thinks it is needed, you will have a CT or MRI scan of the head to check to see if the cancer has spread to your brain.

- If you are able to become pregnant, you will have a blood (about 1 teaspoon) pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a dose level of the combination of vandetanib and everolimus based on when you join this study. Up to 5 dose levels of vandetanib and everolimus will be tested. Up to 3 participants will be enrolled at each dose level. The first group of participants will receive the lowest dose level. Each new group will receive a higher dose than the group before it, if no intolerable side effects were seen at the lower dose. This will continue until the highest tolerable dose of the combination of vandetanib and everolimus is found.

Up to 174 patients will take part in this study. All will be enrolled at MD Anderson.

Study Drug Administration

You will take the study drugs by mouth 1 time every day. The number of pills you will be taking each day will depend on which dose level you are in. The study staff will tell you how many pills you will take and will give you detailed directions on how and when to take the study drugs.

Everolimus should be taken with about a cup (8 ounces) of water, with or without food. Swallow everolimus whole. Do not chew, break, or crush everolimus, unless you cannot swallow it whole. In this case, crush the everolimus tablet and mix it with 2 tablespoons of water if you are not able to swallow it whole.

Vandetanib can be taken with or without food. Do not chew, crush, or break vandetanib. Vandetanib can be swallowed whole OR you can mix vandetanib with water. To do this, mix the pill(s) with 1/4 cup of water for 10 minutes and then drink; then rinse the cup with ½ cup more water and drink.

You will be asked to fill out a pill diary with the times you take everolimus and vandetanib.

The pill diary will be given to you for each study cycle. They should be brought with you to every clinic visit.

Study Visits

At all study visits, you will be asked about any drugs you may be taking and if you have had any side effects.

Within 14 days before Cycle 1:

- You will have a physical exam, including measurement of your weight and vital signs.

- Your performance status will be recorded.
- If it has been more than 3 days since your screening tests, blood (about 2 teaspoons) and urine will be collected for routine tests.

At Weeks 1 and 2 of Cycle 1:

- You will have a physical exam, including measurement of your weight and vital signs.
- Your performance status will be recorded.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- Urine will be collected at Week 1 only

Before Cycle 2 and then before every cycle after that for the first 6 months:

- You will have a physical exam, including measurement of your weight and vital signs.
- Your performance status will be recorded.
- Blood (about 2 teaspoons) and urine will be collected for routine tests.
- Blood (about 1 ½ teaspoon) will be drawn to test your blood sugar.
- You will have an ECG (every 2 cycles).

After you have completed 6 months on study and are tolerating treatment well, you will be seen once per every other cycle.

Before Cycle 3, and then before every odd numbered cycle after that (Cycles 5, 7, and so on):

- Blood (about 2-5 teaspoons) will be drawn to test for fat and sugar levels in the blood. You will need to fast (not eat or drink anything but water) for at least 4 hours before this blood draw.
- You will have an x-ray, CT scan, PET scan, or MRI scan to check the status of the disease.
- If you are able to become pregnant, you will have a blood (about 1 teaspoon) or urine pregnancy test.

You will no longer be able to take the study drugs if the doctor no longer thinks it is in your best interest, if the disease gets worse, or if intolerable side effects occur.

You may choose to stop taking the study drugs at any time. You should tell the study staff or doctor right away if you are thinking about stopping your participation in this study. The study staff or doctor will talk to you about how to safely stop taking the study drugs. You may be asked to return for a follow up visit to check if any side effects happen to you.

End-of-Study Visit

If the study doctor thinks it is needed, you may have an end-of-study visit between 14 and 28 days after your last dose of study drugs. The following tests and procedures will be performed:

- You will be asked about any drugs that you may be taking and if you have any side effects.

- You will have a physical exam, including measurement of your weight and vital signs.
- Your performance status will be recorded.
- Blood (about 2 teaspoons) and urine will be collected for routine tests.
- You may have an electrocardiogram (ECG).
- If you are able to become pregnant will have a blood (about 1 teaspoon) or urine pregnancy test.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. You should discuss these with the study doctor. Many side effects go away shortly after the study drug is stopped, but in some cases side effects may be serious, long lasting, or permanent, and may even result in hospitalization and/or death. If you experience any side effects, the study staff may give you medicines to help lessen these effects.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs.

Vandetanib and everolimus may cause low blood cell counts (red blood cells, platelets, and white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Vandetanib Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • headache • fatigue • skin rash • skin rash/acne • low blood sugar	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• diarrhea • inflammation of the intestines • nausea • abdominal pain • loss of appetite • abnormal liver tests (possible liver damage)

Occasional (occurring in 3-20% of patients)

• abnormal ECG • difficulty sleeping • depression • dry skin • skin sensitivity to sunlight or lamps • itching	• high blood sugar (possible diabetes) • vomiting • weight loss • upset stomach	• abnormal liver tests (possible yellowing of the skin and/or eyes) • weakness • abnormal kidney test • blurry vision • cough

Rare but serious (occurring in fewer than 3% of patients)

• heart failure • irregular/fast heartbeat • stoppage of heart and lung function • severe increase in blood pressure (possible stroke) • brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss)	• stroke • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• inflammation of the pancreas (possible abdominal pain) • lung inflammation (possible difficulty breathing) • stopped breathing • failure to breathe

Vandetanib may rarely cause brain damage, which may cause headache, confusion, seizures, and/or vision loss. The brain damage may or may not be reversible.

Exposure to sunlight while taking vandetanib may cause skin rash. You should avoid direct sunlight. Cover your sun-exposed skin with clothing such as long pants, long sleeve shirts and hats. Use a sun screen that is SPF 45 or higher. You should tell the study doctor when the first sign of a rash occurs, to prevent it from becoming severe.

<u>Everolimus Side Effects</u>

Common (occurring in more than 20% of patients)

• swelling (arm/leg) • fatigue/lack of energy • fever • headache • migraine • anxiety • agitation	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart	• abnormal taste • increased risk of bleeding • low blood cell counts (red, white, platelets) • abnormal liver test (possible liver damage

• aggression • behavioral disturbance • obsessive compulsive symptoms • panic attack • skin rash and/or itching • skin peeling, redness, and/or sores • hives • acne • nail changes • low blood sugar • high blood levels of fat (possible heart disease and/or stroke) • high blood sugar (possible diabetes)	problems, changes in mental status, and/or seizure) • mouth blisters/sores (possible difficulty swallowing) • loss of appetite • weight loss • diarrhea • abdominal pain • nausea • vomiting	• weakness • abnormal kidney test (possible kidney damage) • cough • runny nose • nosebleed • difficulty breathing • infection

Occasional (occurring in 3-20% of patients)

• high blood pressure • chest pain • fast heartbeat • chills • migraine • dizziness • difficulty sleeping • depression • dry skin • breaking of nails • hair loss (partial or total) • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)	• diabetes • dry mouth • inflammation of the stomach and/or intestines • greasy stool • hemorrhoids • bladder inflammation (possible pain and/or urge to urinate) • uterine and/or vaginal bleeding • ovarian cysts (fluid-filled lump) • changed, painful, heavy, or stopped menstrual cycle • pain • muscle spasms	• abnormal sensation (such as pins and needles) • swelling (eyelid) • kidney failure • build-up of fluid around the lungs • lung inflammation (possible difficulty breathing) • life-threatening allergic reaction (such as difficulty breathing, flushing, chest pain, and/or tissue swelling)

Rare but serious (occurring in fewer than 3% of patients)

• build-up fluid in the tissue around the heart sudden stopping of the heart • tissue swelling • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • multiple blood clots (possible organ dysfunction and/or failure) • seizure	• abnormal blood clotting in small blood vessels (possible stroke and/or other organ damage) • destruction of red blood cells (possible kidney damage and/or failure) • blood clot at the site of a graft • progressive multifocal leukoencephalopathy (PML – a disease with brain damage that may likely result in paralysis and/or coma, which may be permanent, or death) • inflammation of the pancreas (possible abdominal pain)	• gallbladder inflammation (possible abdominal pain) • gallstones • low sperm count • inability to have children (males) • decreased kidney function (possible kidney failure) • wound healing problems • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Everolimus may rarely cause you to develop another type of cancer (such as lymphoma [a type of lymph node cancer] and/or skin cancer).

If you have had hepatitis (liver inflammation) in the past, taking everolimus may rarely cause the hepatitis to come back, which may cause death.

You must not drink grapefruit juice or eat grapefruit products while taking everolimus.

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

EKGs/ECHOs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The

scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT and PET scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. A **contrast solution** may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

X-rays send a small amount of radiation though the body. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

Although every effort will be made to keep **study data** safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets during the study and will continue to be stored securely after the study. Only authorized people who are working on this study will have access to study data.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you are able to become pregnant or father a child, you must use appropriate birth control while you are taking the study drugs. Appropriate birth control methods include barrier methods (such as condoms), birth control pills, and a previous vasectomy or hysterectomy. Talk to the study doctor about what kind of birth control you should use.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1 and #2: You are being asked to allow extra blood to be drawn for biomarker and pharmacokinetic (PK) testing. Biomarkers are in the blood and may be related to your reaction to the study drug. PK testing measures the amount of study drug in the body at different time points.

If you agree, blood (about 2 teaspoons) will be drawn for biomarker testing at the following time points:

- Days 1 and 21 of Cycle 1
- Day 1 of Cycle 3
- At any point that the disease appears to get worse

If you agree, blood (about 2 teaspoons each time) will be drawn for PK testing at the following time points:

- Days 1 and 21 of Cycle 1: before you take the study drugs, and then 7 more times over the next 24 hours (8 blood draws)
- Day 1 of Cycle 3, before you take the study drugs (1 blood draw)
- At any point that the disease appears to get worse (1 blood draw)

Optional Procedure #3: You are also being asked to allow a tumor biopsy to be collected to study the possible effect of the study drugs on the tumor tissue. The type of biopsy will depend on where the disease is located. The doctor will tell you more about how your biopsy will be performed and about any risks.

If you agree, this biopsy will be collected 1 time within 14-28 days after you start taking the study drug.

You do not have to agree to the optional procedure(s) in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. The optional procedures will be performed at no cost to you.

Optional Procedure Risks:

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **tumor biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to allow extra blood to be drawn for biomarker testing?

YES NO

Optional Procedure #2: Do you agree to allow extra blood to be drawn for PK testing?

YES NO

Optional Procedure #3: Do you agree to allow a tumor biopsy to be collected to study the possible effect of the study drugs on the tumor tissue?

YES NO

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Sarina Piha-Paul, at 713-563-1930) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. This is important because there may be risks to you if you stop taking the study drugs suddenly or “cold turkey.” The doctor will decide if additional visits are needed to check on your health, such as follow-up visits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you withdraw from the study, the study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Reasons why your participation may be stopped include: if you become pregnant, if intolerable side effects occur, or if the disease gets worse.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

   Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

   To protect your identity, the samples collected from you will be labeled a unique number instead of your name or other identifying information. Only the study doctor or study staff will have access to the code that can link you to your samples.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

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

CONSENT/AUTHORIZATION
(Adult Participants Only)

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SIGNATURE OF PARTICIPANT DATE

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under this protocol.

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

PERSON OBTAINING CONSENT
I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

PERSON OBTAINING CONSENT DATE

PARENT/GUARDIAN PERMISSION

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____

SIGNATURE OF PARENT/GUARDIAN DATE

_____ _____

SIGNATURE OF PARENT/GUARDIAN
Signature of Other Parent (Optional, unless required by the IRB.) DATE

____ The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____ Other parent is deceased, unknown, incompetent, or not reasonably available.

____ Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

_X_ The IRB has determined that the signature of both parents is NOT required.

WITNESS TO PARENTAL/GUARDIAN PERMISSION

I was present during the explanation of the research to be performed under Protocol 2011-0953. The child participant was also present. In my opinion, the parent(s)/guardian provided permission for the child to participate in the research.

_____ _____

SIGNATURE OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

ASSENT OF MINOR

(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other: _____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____

SIGNATURE OF MINOR (Age 13-17) DATE

WITNESS TO ASSENT

I was present during the explanation of the research to be performed under Protocol **2011-0953**. The child participant was also present. In my opinion, the child assented to participate in the research. (Note: If obtaining assent, a witness signature is required.)

_____ _____

SIGNATURE OF WITNESS TO THE ASSENT (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)